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# Science

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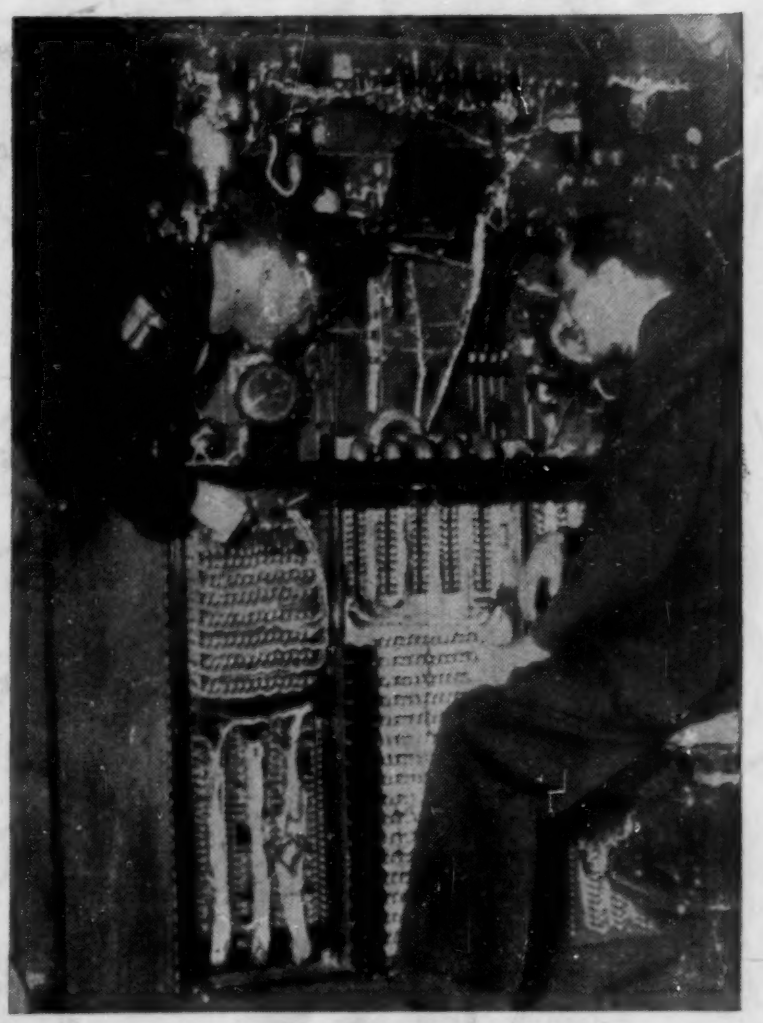

The automatic control panel of the C-54 which recently made the pilotless transatlantic flight being inspected by James L. Anast (*right*), chief of the Army's automatic flight branch of the All-Weather Flying Center, and Capt. Thomas J. Wells (*left*), Army test pilot, of Orlando, Florida, shortly after the plane's arrival at the Brise Norton Aerodrome near London on September 23 (see *News and Notes*).

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## The Polysulfides in Levinstein Process Mustard Gas

# The Polysulfides in Levinstein Process Mustard Gas

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IN WORLD WAR I THE GERMANS HAD THE facilities and materials available to prepare mustard gas by a relatively simple process from thiodiglycol and hydrochloric acid:

$$\underset{\text{Thiodiglycol (TG)}}{HOCH_2CH_2SCH_2CH_2OH} + 2HCl \rightarrow \underset{\text{Mustard Gas (H)}}{ClCH_2CH_2SCH_2CH_2Cl} + 2H_2O. \quad (1)$$

The product of this reaction is referred to in this country as TGH, the symbol H representing mustard gas, bis(β-chloroethyl)sulfide. The materials for this process were not available to the Allies in World War I, but by brilliant teamwork the British and Americans rapidly developed the so-called Levinstein process (named after the British drug manufacturer), the product of which is known as Levinstein H. The method consists in reacting ethylene and sulfur monochloride; the stoichiometry of the reaction is usually written as follows:

$$CH_2 = CH_2 + S_2Cl_2 \rightarrow ClCH_2CH_2SCH_2CH_2Cl + S. \quad (2)$$

When the reaction is allowed to run at about 60°, most of the excess sulfur indicated by this equation precipitates rapidly. If the reaction temperature is held to 35–38°, however, the "excess" sulfur atom does not begin to precipitate until the product has been stored for at least a few weeks. These processes for making TGH and Levinstein H have been reviewed by Sartori (*11*).

The mechanism of the Levinstein process was well understood by Conant (see Sartori, p. 218), but a more complete explanation has recently been found by a research group working at the University of Illinois under Fuson (*6*).

The behavior of the extra sulfur atom in Levinstein H was somewhat of a mystery from World War I to World War II. For a long time it was supposed that the "excess" sulfur was in colloidal suspension, because, as it precipitated, there was very little change in freezing point. Somewhat fanciful suggestions were sometimes offered as to the nature of this colloidal system. The literature, however, does contain suggestions to the effect that the sulfur atom is in chemical combination. For example, Conant, *et al.* (*3*) proposed that part of the sulfur is in the free state, probably colloidal, and the rest in combination as a pentasulfide $(ClCH_2CH_2)S_5$. This suggestion of the presence of a pentasulfide was based on the analysis of the residue from distillation of a sample of Levinstein H. Bennett (*2*) prepared the disulfide $(ClCH_2CH_2)_2S_2$, and Mann, Pope, and Vernon (*9*) isolated a trisulfide $(ClCH_2CH_2)_2S_3$. (The polysulfides will be referred to in this paper as $HS_2$ for the disulfide, $HS_3$ for the trisulfide, etc.)

It is the purpose of this paper to review briefly the part played by Edgewood Arsenal personnel in the elucidation of the mystery of Levinstein H. In order to assist in the interpretation of this work, data are shown (Table 1) which illustrate the nature of Levinstein H as manufactured in steel reactors on a large scale. The composition of a sample is generally determined by distillation under certain specified conditions, with the still-pot at 150° C. under a pressure of about 5 mm. Samples stored in steel containers increase in iron content at a more or less rapid rate.

TABLE 1

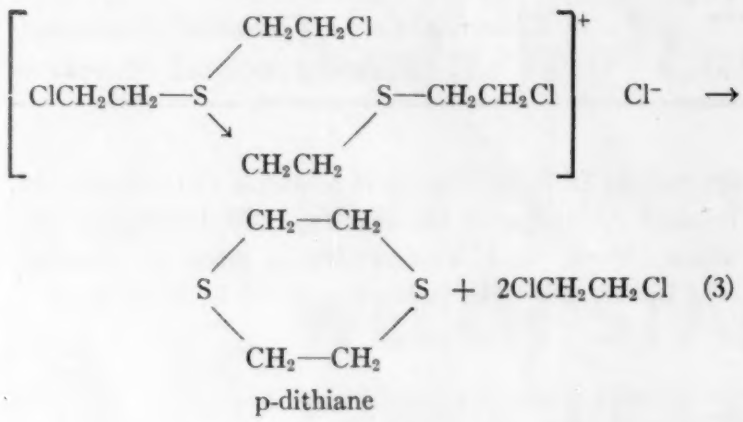
REPRESENTATIVE ANALYSES OF LEVINSTEIN H SAMPLES

| | New sample | Aged sample |
|---|---|---|
| Acidity (as HCl), % | 0.16 | 0.38 |
| Iron (as $FeCl_2$), % | 0.22 | 0.41 |
| Melting point, °C. | 7.7 | 7.6 |
| Density at 20°C., grams/cc. | 1.351 | 1.340 |
| Sulfur, % | 33.46 | 30.70 |
| Chlorine, % | 36.35 | 38.42 |
| Distillation analysis: | | |
| Distillate, % | 78.3 | 76.2 |
| Residue, % | 20.7 | 22.1 |
| Loss, % | 1.0 | 1.7 |
| M.P. of distillate, °C. | 10.2 | 12.1 |
| Purity of distillate*, % | 88.5 | 93.8 |
| Mustard content, % | 69.3 | 71.5 |

* Calculated from melting point, assuming that pure H melts at 14.4° C.

*Contribution of Jarman and Morrison* (*7*): The pure H content of newly made Levinstein H lies in the range of 68–73 per cent by weight. The residue remaining after the distillation of a sample of Levinstein H was fractionally distilled in a 12-plate column; it yielded a fraction of pure H, a quantity of $HS_2$, and some p-dithiane, which condensed in the column. The presence of p-dithiane is probably due to decomposition in the still-pot of sul-

fonium salts which are formed by polymerization of H, as indicated in Equation 3.



p-dithiane

A decomposition of this nature at elevated temperature to give higher homologs of straight-chain thioethers rather than a cyclic compound was recently described by Snyder, *et al.* (*12*), but the mechanism for decompositions of both types was described in 1927 by Bell, Bennett, and Hock (*1*).

In order to eliminate still-pot decomposition as much as possible, several distillations of Levinstein H were made at ordinary temperatures in a molecular still of the type described by Detwiler and Markley (*4*). In one experiment the residue was separated into two fractions by extraction with acetone. Analyses of the fractions gave compositions approximating the formulas $HS_4$ (acetone soluble) and $HS_{12}$ (acetone insoluble). The acetone-soluble fraction, when passed through the molecular still, gave a distillate which contained a considerable proportion of $HS_2$ and a residue with the approximate composition $HS_{4.5}$.

Another sample of whole Levinstein H, when molecularly distilled, gave a residue which separated into two layers of the following compositions:

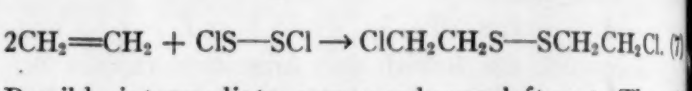
| | %S | %Cl | Approximate composition |
|---|---|---|---|
| Upper layer | 51.89 | 25.27 | $HS_{4.3}$ |
| Lower " | 28.21 | 36.96 | $HS_{1.7}$ |

It has long been known (*5*) that ammonia tends to throw down nearly half of the "excess" sulfur shown in Equation 2. A residue remaining after a molecular distillation of Levinstein H was analyzed before and after such an ammonia-stripping treatment, as shown below. The sulfur precipitate, washed with benzene, acetone, 20 per cent HCl, and water, contained 98.46 per cent sulfur and 0.07 per cent chlorine, by analysis.

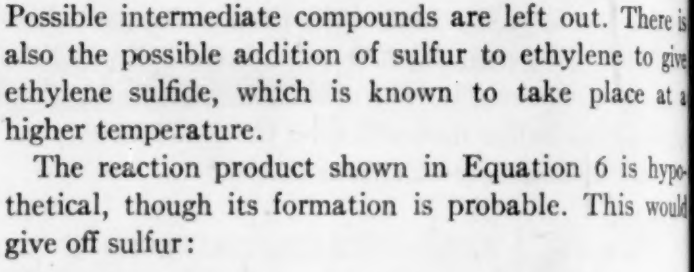
| | %S | %Cl | Approximate composition |
|---|---|---|---|
| Residue before ammoniation | 59.20 | 22.45 | $HS_6$ |
| Residue after ammoniation | 52.44 | 25.55 | $HS_{4.4}$ |

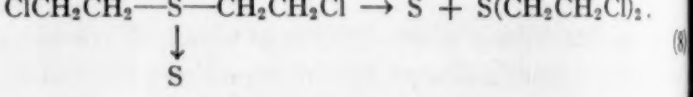
Some exploratory work on the synthesis of $HS_2$ and $HS_4$ was done, but work on this project by these investigators was halted before it was completed. The principal conclusion drawn was that labile polysulfides constitute the major impurities in Levinstein H. They are in a state of constant dynamic flux, based upon the probable property of the linear —C—S—S—C— linkage to acquire and relinquish additional sulfur atoms or molecules under a variety of conditions.

*Contribution of E. Emmet Reid* (*10*): Sulfur monochloride is generally accepted to be an equilibrium mixture in which the following species, at least, are said to be present:



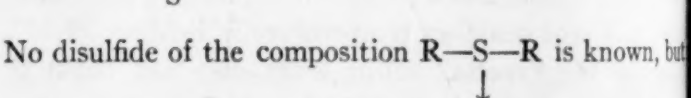
Ethylene may react to all of these:





Possible intermediate compounds are left out. There is also the possible addition of sulfur to ethylene to give ethylene sulfide, which is known to take place at a higher temperature.

The reaction product shown in Equation 6 is hypothetical, though its formation is probable. This would give off sulfur:

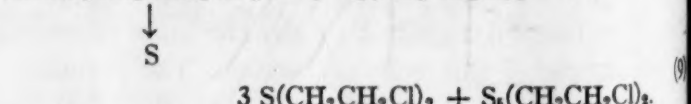


No disulfide of the composition R—S—R is known, but

S

disulfides RS—SR are well known. These take up sulfur to form polysulfides $R_2S_3$, $R_2S_4$, and $R_2S_5$, and the extra sulfur can be taken from them down to the disulfide.

Assuming the Levinstein H to be originally a mixture of the products shown in Equations 6 and 7, we find a compound that gives up sulfur and one that takes up sulfur. Transfer of the S atom would give H and $HS_3$ if the two forms of $HS_2$ were originally in equimolecular proportions. If the ratio were different, the resulting polysulfide would be different; for example:



If the ratio Cl—S—Cl to ClS—SCl can be altered to

S

give a higher percentage of the former, more H should

be formed and there would be more sulfur given off than could be taken up by the disulfide $ClCH_2CH_2S—SCH_2CH_2Cl$. The excess of sulfur would probably precipitate out, as in the 60° process.

If $SCl_2$ can be added so that it takes the extra sulfur from the reaction product of Equation 6 in this manner,

$$ClCH_2CH_2—\underset{\underset{S}{\downarrow}}{S}—CH_2CH_2Cl + SCl_2 \rightarrow S(CH_2CH_2Cl_2) + Cl—\underset{\underset{S}{\downarrow}}{S}—Cl, \qquad (10)$$

the absorption of ethylene can continue without the formation of much of the disulfide $ClCH_2CH_2S—SCH_2CH_2Cl$, which takes up sulfur to give the pentasulfide. All of the polysulfides above the disulfide are to be considered as "statistical" compounds. The composition of a given product may correspond to $R_2S_3$, $R_2S_4$, or $R_2S_5$, but it may be a mixture of all of these, with some disulfide and some free sulfur.

This theory, proposed by Dr. Reid in the fall of 1942, contained the first plausible mechanism for the Levinstein process. Admittedly, it was an armchair theory based on a number of assumptions rather than on laboratory experience, but it served as a useful guide to later work (see reference to Fuson's theory, below, based on a study of the reactions of $HS_2$). The relation between the Reid theory and the composition of Thiokol is obvious:

$$(—CH_2—CH_2—\underset{\underset{S}{\downarrow}}{S}—\underset{\underset{S}{\downarrow}}{S}—)$$

Repeating unit in Thiokol polymer

The dative-bonded sulfur atoms in Thiokol are easily removed by treatment with alkali or sodium sulfide and are easily replaced by milling with sulfur at about 70° C. Of considerable interest, also, is the recent work on the structure of ethylene polysulfides reported by personnel of the Mellon Institute (*13*), who presented experimental evidence for similar structures containing labile sulfur.

*Contribution of Macy* (*8*): This consisted of a study of the probable products of the reaction between ethylene and sulfur monochloride in the light of available data at Edgewood Arsenal with respect to the S and Cl contents of Levinstein H, its freezing point, and its average molecular weight. The structures of the polysulfides arrived at were influenced to a large degree by the Reid theory just described.

The pure H content of Levinstein H lies in the narrow range of about 68–73 per cent by weight, as already stated. The remainder consists of polysulfides. The analysis of the plant product (Table 1) gives close to 33.5 per cent S and 37.1 per cent Cl, in agreement with the stoichiometry expressed by Equation 2.

If all the "excess" sulfur indicated by Equation 2 were to precipitate, it would amount to 16.8 per cent of the total. After Levinstein H has been in storage a few weeks the deposition of sulfur usually starts, and in the course of a few months or a few years the deposit amounts to about 5–8 per cent of the weight of the initial sample. A large volume of data available, however, shows that the deposition does not proceed any further, even under treatment with chemical agents such as ammonia. For example, a sample of Levinstein H, after storage for 25 years in a steel 1-ton container, gave the following analysis: H content by distillation, 76.7 per cent; sulfur (total), 26.8 per cent; chlorine (total), 40.5 per cent. This indicated a deposit of about 6.7 per cent of sulfur in the container. It will be observed that the purity of the sample, with respect to H content, increased as the sulfur precipitated, which is to be expected (also see Table 1). In an effort to explain the composition of the resulting liquid phase, based on this analysis, it was postulated that it consisted of H and a polysulfide of the composition $HS_4$, the final degradation product of a polysulfide $HS_6$.

$$ClCH_2CH_2\underset{\underset{S}{\downarrow}}{S}—\underset{\underset{S}{\downarrow}}{S}CH_2CH_2Cl \qquad ClCH_2CH_2\underset{\underset{S}{\downarrow}}{\overset{\overset{S}{\uparrow}}{S}}—\underset{\underset{S}{\downarrow}}{\overset{\overset{S}{\uparrow}}{S}}CH_2CH_2Cl$$

$HS_4$ $\qquad$ $HS_6$

On the basis of the H content in the above analysis, and assuming $HS_4$ as the principal impurity, the calculated sulfur content is 27.0 per cent, in close agreement with the experimental value. Separation of sulfur from the higher polysulfides to form the lower polysulfides would not affect the freezing point. *Constancy of freezing point was one factor which led to the original belief that the sulfur is present in colloid form.*

These considerations led to the postulate that freshly prepared Levinstein H, which contains about 70 per cent by weight of H, will also contain 30 per cent of polysulfides represented by $HS_6$, and that the polysulfides lose S slowly to the $HS_4$ level. It was also postulated that polysulfides higher than $HS_6$ may exist, the additional S atoms being extended as side chains on those already present in $HS_6$.

Support for the proposal that the polysulfides in Levinstein H are at least $HS_6$ was obtained by a study of available freezing point data such as are shown in Table 2. Column III gives the H content of the sample as determined by the usual distillation analysis illustrated in Table 1. In order to determine the H content more rapidly, it was at one time the practice to determine the freezing point and apply Raoult's law, $\Delta t = K N$, where $\Delta t$ is the depression in freezing point; N, the mole fraction of impurity; and K, the constant for pure H (the value of which is 36.4). For a long time it was

thought that the principal impurity in Levinstein H was chloroethyl chlorovinyl sulfide, the molecular weight of which is 157. The data obtained, assuming the impurity to have a molecular weight of 157, are considerably at variance with the H contents determined by distillation. In column IV the data obtained, assuming the impurity to have a molecular weight of 319 (that is, $HS_6$), are in quite good agreement with distillation data. The agreement of H content by distillation, and H content by

TABLE 2

FREEZING POINT AND H CONTENT OF LEVINSTEIN H

| I No. of runs | II Average F.P.* (°C.) | III Net H by distillation | IV Net H by F.P.† |
|---|---|---|---|
| Edgewood Arsenal Manufacture, 1918 | | | |
| 1 | 4.0 | 67.3 | 55.3 |
| 17 | 7.16 | 71.1 | 66.6 |
| 1 | 7.8 | 72.4 | 69.0 |
| 10 | 8.09 | 71.2 | 70.2 |
| 7 | 8.67 | 72.4 | 72.5 |
| 1 | 10.0 | 73.6 | 78.1 |
| Edgewood Arsenal Manufacture, 1937 | | | |
| 1 | 4.25 | 58.7 | 56.2 |
| 5 | 6.30 | 65.8 | 63.4 |
| 9 | 6.76 | 66.9 | 65.1 |
| 3 | 7.16 | 67.5 | 66.6 |
| 1 | 7.82 | 65.3 | 69.0 |
| 2 | 8.27 | 67.8 | 70.9 |

* Averages of data with maximum spread of 0.5° C.

† Calculated from Raoult's law, assuming impurity with M.W. = 319.

freezing point, assuming the polysulfide impurity to average $HS_6$, is shown graphically by curve AA in Fig. 1.

It can be calculated from Raoult's law that a Levinstein H sample with an H content of 72.5 per cent and a freezing point of 9.05° (Fig. 1) contains an impurity with an average molecular weight of 351, which corresponds to $HS_7$.

The line BB of Fig. 1 is of interest in that it shows how the H content of plant samples can be determined to within a few per cent by means of the freezing point after the data have been obtained for a comparatively few samples. The lower portion of the line gives data obtained in certain tests to determine storage stability of Levinstein H in steel munitions under tropical conditions. Levinstein H decomposes fairly rapidly under these conditions, but in the first stages of the decomposition there is a rapid decrease in freezing point with relatively small decrease in H content. This indicates that the polysulfides decompose first by disproportionation. The data for the plant samples obtained in 1937 apparently fall on a line parallel to BB but displaced slightly to the left of it.

The decomposition of Levinstein H in small steel containers is remarkably rapid under tropical conditions (100–150° F.), probably due to the oxidizing nature of the sulfur in the polysulfides, $Fe + \ddot{S}: \rightarrow Fe^{++} :\ddot{S}^{=}$ and subsequent reaction with ionic species in mustard similar to those indicated by Equation 3 and postulated by Bell, Bennett, and Hock (*1*). On the other hand,

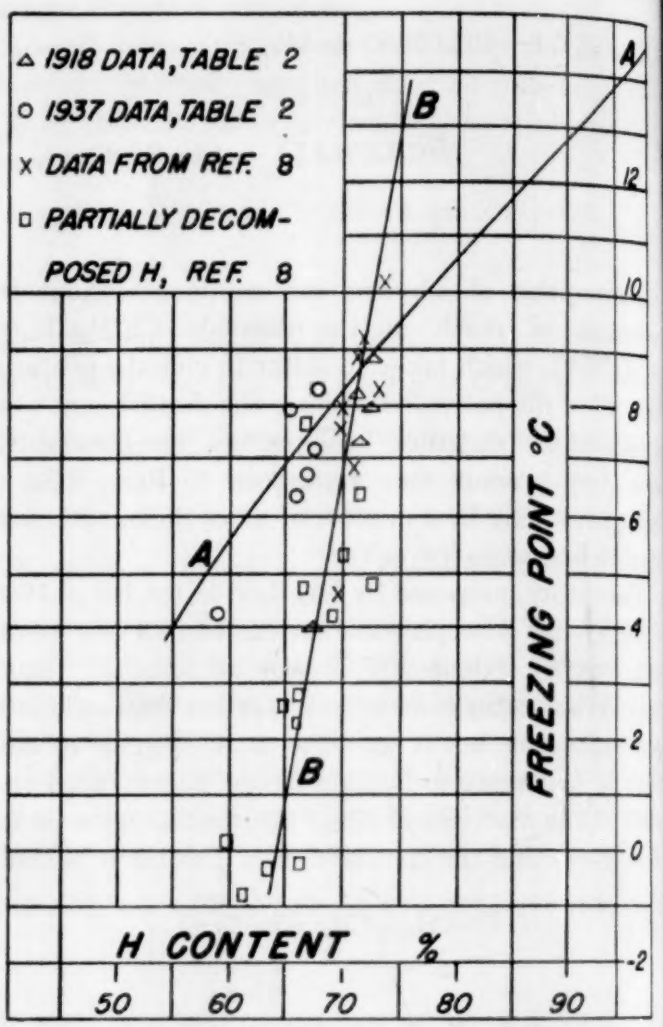
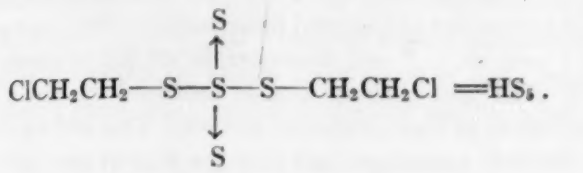



FIG. 1. Curve AA—Relation between freezing point and H content of Levinstein H according to Raoult's law for impurity with molecular weight of 319. Line BB—Freezing point and H content of plant runs of Levinstein H.

Levinstein H is quite stable toward aluminum, the tight aluminum sulfide coat formed by oxidation with the polysulfides apparently giving the same sort of protection that is afforded by aluminum oxide.

A result which at first appeared to be quite startling was the fact that, when samples of Levinstein H have decomposed in steel containers to the extent that very little pure H can be found by distillation, the material is even more vesicant than the original samples. It was suggested to Dr. Fuson at the University of Illinois, through OSRD channels, that the tarry decomposition products may contain higher homologs of mustard, which are known to be more vesicant and that the products obtained by heating mustard would be worthy of study. The result of this work was reported recently by Fuson (*6*), who found such homologs and points out that the mechanism of such decomposition by mustard had been thought out nearly 20 years ago by Bell, Bennett, and Hock (*1*).

*Current status due to Fuson, et al.* (*6*): The Edgewood Arsenal postulates were summarized (*8*, *10*) in June 1943. Intensive work on the isolation and properties of the polysulfides in Levinstein H was undertaken not only by Fuson's group at the University of Illinois but also by British investigators. Both sets of investigators reached the conclusion that $HS_2$ does not sulfurize readily (the basis of the Edgewood theory) but that $HS_3$ does add sulfur easily and is the structurally important unit among the polysulfides:



Fuson (and British workers) assume that the —S—S—S— unit in $HS_3$ adds more sulfur at the central atom. The polysulfide generally present in highest concentration in Levinstein H newly made is $HS_7$, but all these higher polysulfides lose sulfur readily down to the stable $HS_5$ level with is illustrated here. This new conception is quite different from the well-known Thiokol two-in-line structure described earlier in this article.

The Edgewood theory assumed that polysulfides of H are built up on the $HS_2$ unit. Fuson, in experiments designed to find out how $HS_2$ disappears in the Levinstein process, discovered that it reacts with sulfur monochloride to yield $S_3Cl_2$ as a most important product. This reacts with ethylene in the Levinstein process

$$2C_2H_4 + S_3Cl_2 \rightarrow ClCH_2CH_2S_3CH_2CH_2Cl$$

and the $HS_3$ is sulfurized by the $S_2Cl_2$ present to higher polysulfides. For further details on a brilliant piece of work the reader is referred to the papers by Fuson and his associates (*6*).

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# Starring in *American Men of Science*


**Stephen S. Visher**

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IN 1903 J. McKEEN CATTELL, THEN PROfessor of psychology at Columbia University and editor of *Science*, undertook to prepare a list of the 1,000 most significant living American scientists. The methods which he used were, in brief, as follows:

Ten outstanding leaders in each of 12 sciences were asked to list in order of merit the leading research scientists in their science. These 120 judges were well distributed geographically, represented several different educational institutions, and were considered to have good judgment. From their lists, Cattell worked out the average rank of each of the scientists voted upon. The number selected in each science to make up the 1,000 was approximately one-fourth of the number of such scientists then productive in America. Biographical sketches were obtained of all the scientists of 1903 judged worthy of sketching in a biographical directory. When the first *American men of science* was published in 1906, asterisks were inserted to indicate the 1,000 leaders. The directory proved so widely useful that later editions were issued in 1910, 1921, 1928, 1933, 1938, and 1944. These successive editions contained an increasing number of sketches—approximately 4,000, 5,500, 9,500, 13,500, 22,000, and 34,000, respectively.

For the second edition, voting on starring was done by all living starred scientists who would cooperate. For subsequent editions, all those nominated by a number of persons as meriting starring also were asked to vote.

The decision as to which fields of work were to be recognized by the starring of leaders was made personally by Cattell. He chose anatomy, anthropology, astronomy, botany, chemistry, geology, mathematics, pathology, physics, physiology, psychology, and zoology. Thus, even the most eminent workers in other fields were not eligible for a star. Moreover, a man who worked between well-recognized fields—in biochemistry, geophysics, or astrophysics, for example—or whose work overlapped two or more sciences, as does that of many ecologists and biologists, was rarely starred unless highly distinguished.

Another arbitrary decision made by Cattell was that few workers in applied or "practical" sciences were classed as meriting sketching in *American men of science*. This is significant because in 1903 the number of persons to be starred in any field was, it will be recalled, approximately one-fourth of the number judged worthy of a sketch in the directory.

An especially significant decision by Cattell was that during his lifetime (he died in 1944) no change should be made in the system of starring after the third edition, and that new stars should be added only in such numbers as to preserve the percentages assigned to each science in 1903. Thus, there was no adjustment to the differential growth of the several sciences. Because the number of scientists grew much more rapidly than the number of stars allowed, the proportion of scientists starred has decreased rapidly. (One thousand were starred in 1903 and approximately 250 for each later edition except the third (1921), in which 351 were starred.) For example, in 1943 about 34,000 scientists were judged worthy of sketching, but only 256 were newly starred, or approximately 1/32 as many as there were scientists newly sketched in *American men of science* since the previous starring. The total number of scientists newly starred in the fourth to seventh editions, inclusive, was about 1,000, or only 1/25 of the number who attained in those years sufficient scientific standing to be judged worthy of sketching.

In brief, while in 1903 about one-fourth of the scientists were starred, in 1943 fewer than 1/25 of those who were not elderly were starred. In some fields—chemistry, for example—less than 2 per cent of the research workers under age 60 were starred, as against about 25 per cent in 1903.

Another unfortunate consequence of using almost the same basis for starring for nearly 40 years resulted from the multiplication of scientific publications. Because of the much greater output and specialization, few men are now competent to evaluate the work of any large share of the younger men in their science. Most of the 12 sciences of 1903 now have several well-separated divisions, some of which include more active research workers than the entire science had in 1903.

## On the Significance of Starring

Despite imperfections of methods of starring, it is considered by numerous competent men to have been a notable contribution to scientific progress. The following summary, from a study of starred psychologists (*Amer. J. Psychol.*, 1939, **52**, 278–292), is quotable in this connection:

> Cattell's inauguration of the system of starring the leading research workers in each of 12 fundamental sciences is considered by competent judges to have been a major contribution to the growth of research in America.

The star indicates that, in the private opinion of his peers, the starred scientist is distinguished for research. It implies either a large volume of good work or a considerable amount of especially original work. Of course it does not imply that the work done by others is not decidedly worth-while, but merely that it has not impressed the voters as quite so worthy of approbation.

The star is a recognition which not only gives the recipient satisfaction, but also increases his opportunities. It is a challenge to the recipient to continue his good work and to others who aspire to win this recognition. Vast amounts of good work have been completed as a result of this friendly rivalry. Many scientists who are not starred feel confident that they are "as good a man as . . . " and consequently set out to prove it.

The good that starring does is increased by the widened knowledge as to who are starred and why. This widened knowledge not only encourages and puts the starred men more fully on their mettle, but it also attracts attention to their work and increases their opportunities for further research. It, moreover, augments the opportunities of promising persons not starred in the hope that, as a consequence of encouragement and improved facilities, they will win this coveted recognition. The various universities employing starred scientists are placing increased value upon this recognition as a proof of individual merit and institutional strength. They not only attempt to retain and attract men already starred, but also to have local men not yet starred win this high honor; to this end they often increase facilities and otherwise encourage their more promising men.

Among the 770 starred scientists whose replies to a recent questionnaire expressed opinions as to the influence of the star on their own careers, nearly three-fourths reported that the star "improved their status" (231 slightly, 141 moderately, and 34 notably). Most of the 160 who reported no improvement were starred late in life. (A considerable number specifically stated that their stars came too late.)

More than three-fourths of those reporting considered that "starring has in general been beneficial" (135 slightly, 286 moderately, 142 notably). Only 6 considered starring harmful.

## The Desirability of Broadening the Basis for Starring

According to nearly nine-tenths of those replying, starring would be beneficial "if in the future stars are awarded to the top 10% of the workers active in research in numerous fields (not only the present 12), by secret vote of the top third or so of the active workers in that field." (One hundred twenty-five voted "decidedly beneficial," 185 "moderately," 145 "slightly." Only 57 considered it would be inconsequential or undesirable.)

The increased specialization, which is almost unavoidable as knowledge accumulates, makes it increasingly desirable that those persons who are qualified to judge the merit of achievement in any particular field do so.

The secret balloting by competent experts should be extended to numerous additional fields. Aside from the encouragement that such recognition affords, another major advantage of such rating by secret ballot of those high in a wide variety of fields is that it increases the prospect that those who are judged outstanding will be given better opportunities to use their special talents and skills in the making of a better world. This happens partly because universities and other institutions dedicated to human betterment actively desire assistance in locating persons of especial merit so that they can obtain their services. Hence, the extension of starring to numerous fields not now represented would be highly advantageous and would certainly result in increased achievement.

Not only have nine-tenths of the 770 starred scientists who recently voted on the matter approved of a broadening of the basis for starring and expressed the conviction that the consequences would be advantageous, but large numbers of nonstarred scientists and persons who employ scientists have expressed similar opinions. It therefore appears that in the eighth edition of *American men of science*, now in preparation, many more persons should be starred than in the previous editions. Moreover, the voting should be done in fields small enough so that those selected to vote are better qualified to rate the younger workers than is possible when the fields are large and diversified (all of zoology, for example, or all of chemistry). This will mean extra work for those who arrange for and assemble the votes and for the publishers, but the benefits should abundantly justify the extra efforts.

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# NEWS *and Notes*

**The Army's electronically-controlled C-54** recently used to demonstrate pilotless flight across the Atlantic was first developed early in 1946 and since then has been used on many shorter hops within the United States. From the time the flight commander, Col. J. M. Gillespie, set the automatic controls into action on the runway of the Newfoundland airport at Stephenville, it was not necessary for him or his crew to direct the flight in any way. Signals from two radio transmitters, located on ships at sea along the course of the flight, were interpreted by the plane's radio compass, and a third set of signals from a transmitter on a truck at the British airport brought it in for an automatic landing.

The 14 passengers making this initial flight included several U. S. scientists and an observer from the RAF.

## About People

**S. H. Katz,** senior consultant, Chemical Corps Technical Command, Army Chemical Center, Maryland, is visiting England and Germany to investigate work on Chemical Warfare Protective Equipment. His investigation will cover materials, manufacturing processes, testing, and the theoretical aspects.

**Allan D. Maxwell,** formerly of the Nautical Almanac Office, U. S. Naval Observatory, has been appointed professor of astronomy, Howard University, Washington, D. C.

**R. L. Meier,** research chemist, California Research Corporation, has been appointed executive secretary, Federation of American Scientists, Washington, D. C., for one year to succeed **William Higinbotham.**

**Arthur B. Bromwell,** Northwestern University, was appointed secretary, American Society for Engineering Education, effective October 1. The headquarters of the Society will be moved from the University of Pittsburgh to Northwestern University.

**Bowen C. Dees,** assistant professor of physics, Rensselaer Polytechnic Institute, has been appointed physicist, Economic and Scientific Section of Gen. MacArthur's organization in Tokyo. In this position, Dr. Dees will survey and advise concerning the physical research being conducted in university and commercial laboratories in Japan.

**Marjorie T. Bingham,** formerly botanist, Cranbrook Institute of Science, has been appointed assistant professor of biology, Northern Michigan College of Education, Marquette.

**C. Lee Huyck,** professor and head, Division of Pharmacy, Columbia University College of Pharmacy, has resigned in order to become director, Department of Pharmacy, Howard College, Birmingham, Alabama.

**Jacques Rousseau,** director, Montreal Botanical Garden, has recently returned from a botanical survey in the interior of the Ungava Peninsula. Dr. Rousseau traveled by canoe from the source of George River to its mouth and crossed that peninsula from Seven Islands on the St. Lawrence River to the Ungava Bay.

**Alexander Brunschwig,** formerly professor of surgery, University of Chicago, has been appointed head, Department of Surgery, Memorial Hospital, Center for Cancer and Allied Diseases, New York City. Dr. Brunschwig also holds the concomitant appointment as professor of clinical surgery, Cornell University Medical College.

**George A. Edwards,** Harvard University, has been appointed assistant professor, Department of Biology, Tufts College, Medford, Massachusetts.

**Frederick C. Frick,** Columbia University, and **Moncrieff H. Smith,** Stanford University, have been appointed instructors in psychology at Harvard University.

**Ethel Melsheimer Miller,** librarian of the Botany and Zoology Library, Ohio State University, and of the Ohio Academy of Science, retired September 30. Mrs. Miller established the Botany and Zoology Library in 1917.

**Marshall Clagett,** instructor in history, Columbia University, has been appointed assistant professor, Department of the History of Science, University of Wisconsin.

**Irving A. Denison,** who has been connected with the Soil Corrosion Section, National Bureau of Standards, since 1929, has been appointed chief of the Bureau's Underground Corrosion Section.

**Noel Elmer Foss,** technical director, Department of Pharmacy, Calco Chemical Division, American Cyanamid Company, Bound Brook, New Jersey, has been appointed assistant dean, College of Pharmacy, University of Illinois.

**Kenneth N. Ogle,** formerly professor of research in physiological optics, Research Division, Dartmouth Eye Institute, Hanover, New Hampshire, has become a member of the permanent staff, Division of Physics and Biophysical Research, Mayo Foundation and Mayo Clinic, Rochester, Minnesota, where he will continue research in physiological optics and visual problems and carry on clinical researches in collaboration with the Section on Ophthalmology.

**Robert J. Ollry,** formerly a teacher at St. Lawrence University, has been appointed associate professor of biology and acting chairman, Department of Biology, Norwich University, Northfield, Vermont.

**Max Hansen,** formerly director of research, Durener Metallwerke, Duren, Germany, and a leading nonferrous physical metallurgist, has been appointed associate professor of metallurgical engineering, Illinois Institute of Technology.

**J. A. Stekol**, Amino Products Division, Rossford, Ohio, and **Denis R. A. Wharton,** Cornell University Medical College, have been appointed to the staffs of the Lankenau Hospital Research Institute, and the Institute for Cancer Research, Philadelphia.

**William D. Gray,** formerly chief, Biological Laboratories, U. S. Quartermaster Depot, Jeffersonville, Indiana, has been appointed associate professor, Department of Botany, Ohio State University.

**Cecil A. Gibb,** University of Sydney, Australia, has been appointed half-time visiting lecturer in the Department of Psychology, University of Illinois.

**Hubert Bleier,** who succeeded **Erich von Tschermak** at the School for Agriculture, Vienna, has informed **Lester W. Sharp,** Cornell University, that he was compelled to flee from Austria to Germany in 1945 and suffered the loss of all his possessions, including his scientific library. Prof. Bleier, who has now found employment in a seed improvement company, where he is carrying on researches on polyploid rye, would deeply appreciate the donation of any books, separates of articles in the fields of cytology, genetics, and agriculture, together with any other publications which would in some measure compensate for the loss of his library and that of the company with which he is associated. They may be sent in care of F. von Lochow-Petkus, 20a Bergen (Kreis Celle), Postschliessfach 5, Germany (British Zone).

## Grants and Awards

**Corrosion research** being carried on in the Department of Chemistry, University of Texas, under the direction of **Norman Hackerman** is being supported by grants from the Office of Naval Research and the Natural Gasoline Association of America. Under the Navy grant **Don Marshall** and **Aubrey McClelland** will work on passivity of metals, especially chromium and stainless steel, and **John Sudbury** will carry out fundamental research on the mechanism of corrosion inhibitor action. The other grant provides for work being done by **E. E. Glen** on the mechanism of corrosion inhibitors, particularly in anaerobic systems.

**The Kirksville College of Osteopathy and Surgery,** Kirksville, Missouri, has received a $6,119 grant from the National Institute of Health to be used in support of the work of **J. S. Denslow,** director of research, who is studying the spatial relationship of muscle fibers in single motor units.

**The Poultry and Egg National Board** has announced that nominations are solicited for the Christie Award of $500 and a scroll, which will be presented at the annual meeting of the Board in Chicago in January of 1948. This award, made possible through a donation from Andrew Christie, will be presented each year for the next 5 years. The recipient will be the person who has made the greatest contribution in the past 10 years through research, teaching, or extension in the interpretation of scientific results or prosecution of research dealing with the determination, preparation, conservation, or improvement of the nutritive properties of poultry and eggs. Contributions must have served to enlighten the public regarding the value of poultry and eggs in the human diet or to increase the knowledge of the quality and nutritive value of poultry products. Further information may be obtained from the chairman of the Christie Award Committee, J. Holmes Martin, Purdue University, West Lafayette, Indiana.

**Thomas H. Johnson,** chief, Ballistic Measurements Laboratory, and associate director, Ballistic Research Laboratories, Aberdeen Proving Ground, Maryland, during the war, and now head of the Physics Section, Brookhaven National Laboratories, received the Medal for Merit, the highest civilian award for war work from the Government, on September 25, in recognition of his outstanding wartime leadership in the development of highly accurate techniques for the measurement of the blast and fragmentation effects of bombs and in the development of microwave techniques for measuring velocities of projectiles, both in the bore of the gun and in flight.

**Moses J. Eisenberg,** chief, Dental Services, Jewish Memorial Hospital, Boston, and formerly research fellow in dentistry, Harvard University, was the recipient of the First Award for his exhibition at the recent Boston meeting of the American Dental Association. The award was given for original research in a basic science. Dr. Eisenberg's field is histology.

## Fellowships

**The General Electric Company** has announced that applications are now being accepted for the academic year 1948-49 for grants under the $1,000,000 G-E Educational Fund which include the Charles A. Coffin Fellowships, awarded in the fields of electricity, physics, and physical chemistry, and the Gerard Swope Fellowships, first granted in 1946, awarded in the fields of industrial management, engineering, physical sciences, and any other scientific or industrial field. The fellowships will be granted for the amount needed up to a maximum of $1,500 annually for each individual. A grant of $500 may be made for specific apparatus or other expense in connection

with the research work. In addition, in case of need, loans up to $1,000 may also be made. The fellowships are intended for graduates who need financial assistance and who have shown by the character of their work that they could with advantage undertake or continue research work in educational institutions either in this country or abroad. They are not intended for graduates who now hold, or expect to hold, any other fellowship which carries a stipend larger than the tuition at the institution where the research work is to be done. Applications, which must be filed by January 1, 1948, may be obtained from A. D. Marshall, secretary, General Electric Educational Fund, Schenectady, New York.

## Colleges and Universities

**The School of Medicine, Louisiana State University,** has appointed **Harry E. Dascomb** instructor in medicine, **Robert M. Waters** instructor in surgery, **John J. Blasko,** clinical instructor in neuropsychiatry, **Louis Raider,** clinical instructor in radiology, **Simon V. Ward, Jr.,** clinical instructor in obstetrics and gynecology, **Harold S. Gamble** assistant in anatomy, **John D. Krafchuk** assistant in microbiology, **James T. McQuitty,** clinical assistant in surgery, and **Robert D. Bone,** clinical assistant in medicine. The school year has been expanded from 32 to 36 weeks.

**A Department of Bacteriology** was created July 1 on the Bloomington campus of Indiana University, having as its chairman **L. S. McClung,** associate professor. Instruction and research in bacteriology had been combined with botany since 1940. In the same Department, **S. E. Luria,** assistant professor, has been promoted to associate professor; **I. C. Gunsalus,** Cornell University, has been appointed professor and will have charge of a program relating to bacterial physiology and metabolism; **Herbert J. Welshimer,** Ohio State University, has been appointed instructor; **C. F. Robinow,** Strangeways Laboratory, Cambridge, has been appointed visiting professor during the spring semester and will give an advanced course in bacterial cytology; and **Charles Russell** and **Renato Dulbecco** will serve as research associates. Research in the Department will be supported in part by grants from the National Institute of Health and the American Cancer Society.

**At the Marine Laboratory, University of Miami,** Coral Gables, Florida, **Craig A. Gathman,** who has been appointed research associate in fisheries biology, is collaborating with **F. G. Walton Smith,** director of the Laboratory, in a study of the British Honduras fisheries carried out on behalf of that government. **Luis Rivas,** recently named associate professor of zoology at the University, is working on the taxonomy of West Indian marine fishes, a work which, it is hoped, will greatly add to the reference collection of Florida and West Indian marine fish at the Marine Laboratory; and **Charles C. Davis,** newly appointed assistant professor of zoology, is studying the plankton as part of a comprehensive ecological survey of the inshore waters near Miami.

**The Geological Museum of the University of Minnesota** has purchased from F. W. Sardeson his private collection of fossils which contains about 3,300 species, each being represented by from 1 to 100 specimens. Dr. Sardeson collected most of the specimens over a period of 50 years from the Ordovician rocks of Minnesota, Wisconsin, and Iowa. The collection also contains Jurassic invertebrates which Dr. Sardeson collected in central Europe while a student at Heidelberg.

## Industrial Laboratories

**Sharp & Dohme, Inc.,** has announced the following staff changes following a meeting of the Board of Directors: **John S. Zinsser,** president and chief executive officer, elected chairman of the Board; **William L. Dempsey,** executive vice-president, elected president to succeed Mr. Zinsser, who will continue as chief executive officer; and **William A. Feirer,** formerly vice-president in charge of medical research, elected executive vice-president and a director of the Company.

**Maurice L. Moore,** assistant director of research, Frederick Stearns & Company, has been appointed director of the Research Laboratories of Smith, Kline & French, Philadelphia, to succeed the late **Walter G. Karr.**

**General Electric Corporation** has recently developed, under the direction of **D. E. Bovey** in its General Engineering and Consulting Laboratory, a "metals comparator" which, by employing an electronic circuit, discriminates between the metal in question and a standard sample. Paint, polish, or rust on the metal does not affect its accuracy. It is expected that the device will prove useful in the inspection for quality of assembly line parts and in the rapid sorting of supplies of metal objects without damage to the metals.

**Eastman Kodak Company** has recently prepared a quantity of isotopic methyl iodide in its Synthetic Organic Research Laboratory. This chemical compound contains "tracer" $C^{13}$ in an improved and highly usable form which does not require further extensive treatment before actual use, as did the previous heavy carbon produced by Kodak. The method used in making the new compound was one first used at the University of California in the preparation of compounds containing radioactive carbon. The National Research Council has received the first shipment of methyl iodide and will distribute it and later shipments to qualified research organizations.

## Meetings

**The American Mathematical Society** will hold its 428th meeting at Hunter College, October 25, beginning at 10:00 A.M. Section I, on Analysis, in Room 1217, will hear papers by I. E. Segal, Institute for Advanced Study; Paul Erdös, Syracuse University; J. C. Oxtoby, Bryn Mawr College; Everett Pitcher, Lehigh University and Institute for Advanced Study; Arthur Sard, Queens College; and R. J. Duffin, Carnegie Institute of Technology. At the meeting of Section II, on Algebra, Topology, and Logic, in Room 1239, papers will be presented by O. E. Glenn, Lansdowne, Pennsylvania; G. C. Webber, University of Delaware; Saunders MacLane, University of Chicago; L. V. Toralballa, Fordham University; E. H. Spanier, Institute for Advanced Study; Hing Tong, National Research fellow, Institute for Advanced Study; and Ira Rosenbaum, Brooklyn College. A general session, to be held at 2:00 P.M. in the High School Auditorium, will feature a lecture on "Global Theorems in Riemannian Geometry" by C. B. Allendoerfer, Haverford College.

**The National Academy of Sciences** will hold its autumn meeting November 17–19 at 2101 Constitution Avenue, Washington, D. C. The sessions on Monday will be devoted to a discussion of the functions of the Academy with reference especially to its relations to the Govern-

ment and other groups and to the character of its scientific sessions. Scientific papers will be presented at the morning and afternoon sessions on Tuesday, and the morning session on Wednesday. The Public Lecture will be given Monday evening at 8:30 in the Academy Auditorium, and the Academy Dinner will be held Tuesday evening at the Hotel Washington at 6:30. F. E. Wright, Geophysical Laboratory, Carnegie Institution of Washington, is chairman of the Local Committee on Arrangements.

**The American Philosophical Society** will hold its autumn general meeting November 20–21 in Philadelphia. At the open sessions on these two days, beginning at 10 A.M. Thursday, papers will be read by: Lyman H. Butterfield, Leonard Carmichael, Wallace O. Fenn, Paul D. Foote, Werner Jaeger, Chester S. Keefer, Hayward Keniston, William L. Langer, O. E. Neugebauer, William G. Roelker, Carl O. Sauer, Robert L. Schuyler, Harlow Shapley, Sumner H. Slichter, Mark Starr, Francis R. Steele, Vincent du Vigneaud, and William L. Westermann. On the evening of November 20 Douglas S. Freeman will give the Franklin Medal Lecture on the subject of recent discoveries concerning George Washington.

**The annual meeting of the Society of Rheology** will be held October 30–November 1 at the Hotel Pennsylvania, New York City. The program follows: Friday morning, "Measurements of Stress Relaxation in High Polymer Materials," W. S. Macdonald and Alexis Ushakoff, W. S. Macdonald Company, Cambridge, Massachusetts; "Rheological Properties of Polystyrene," Rolf Buchdahl, Monsanto Chemical Company, Springfield, Massachusetts; and "Viscous Flow of Molten Polystyrene," R. S. Spencer and R. E. Dillon, The Dow Chemical Company, Midland, Michigan; Friday afternoon, "The Cragoe L Function for Viscosity of Oils Under Pressure at Certain Temperatures," R. B. Dow, Bureau of Ordnance, Navy Department, Washington, D. C.; "The Viscosity Basis of Plasticizer Action," H. Jones and E. Chadwick, Plastics Division, The Geigy Company, Ltd., Manchester, England; "Viscosity and Shear Elasticity Measurements of Liquids by Means of Shear Vibrating Crystals," W. P. Mason, Bell Telephone Laboratories, Murray Hill, New Jersey; and the annual business meeting at 3:45 P.M. A social program in the evening will include color movies by K. Compton, Bell Telephone Laboratories. Saturday morning, "Theory of Plastic Flow Versus Theory of Plastic Deformation," W. Prager, Brown University; "Anomalous Viscosity of Aluminum Soap-Benzene Gels," Walter H. Bauer, Henry Raich, and Grant K. Rauscher, Rensselaer Polytechnic Institute; "New Aspects of Colloid Science to Rheology," Ernst A. Hauser, Massachusetts Institute of Technology; and "Pseudoplastic Flow Properties of Lyophilic Colloids," Earl K. Fischer and Charles H. Lindsley, Institute of Textile Technology, Charlottesville, Virginia.

**The IXth General Assembly of the International Union of Biological Sciences** was held in Copenhagen July 28, 1947, with participation of representatives of UNESCO and of the International Council of Scientific Unions (ICSU), and delegates of the following countries: Belgium, Brazil, Bulgaria, Czechoslovakia, Denmark, France, Great Britain, Holland, Mexico, Morocco, Norway, Poland, Spain, Sweden, Switzerland, United States. The representative of China, delayed, sent his regrets from Marseille in not being able to arrive in time. Prof. Borel, vice-president of ICSU, was present at the Assembly, which was of particular importance. Actually the General Assembly had not been able to be convened since 1935 as a consequence of world events. Revised statutes were therefore adopted by the Assembly, and new activities were undertaken appropriate to new circumstances.

The new Bureau was thus constituted: president: M. J. Sirks, Genetisch Institut, Huis de Wolf, Haren (Gron.), Holland; vice-president: H. Munro Fox, Department of Zoology, Bedford College for Women, Regents Park, London N.W.1, England; secretary general: P. Vayssiere, Museum d'Histoire Naturelle, 57 Rue Cuvier, Paris Ve, France; associate secretary general: **Stuart Mudd,** School of Medicine, University of Pennsylvania, Philadelphia 4; treasurer: F. Chodat, Institut for General Botany, University of Geneva, Switzerland.

Joseph Needham, representing UNESCO, in agreement with A. Establier, representing ICSU, indicated that the great international organization of UNESCO attached a very special importance to the activities and investigations pursued by the Unions, and that UNESCO would aid in their realization, it being understood, however, that the maintenance of the Unions themselves must be assured by their own resources. In brief, these international Unions are self-sustaining organizations supported by contributions from adhering nations. Substantial sums from UNESCO will be distributed, however, through these Unions as grants-in-aid or subventions to particular projects.

The creation of new Sections was planned—Experimental Cytology, Embryology, Entomology, Genetics, Microbiology, Zoology—and also several mixed Commissions, such as Radiobiology, Natural Calamities, Oceanography. These last Commissions should comprise members of other Unions. The Executive Committee, which convened on October 2, was to assure the carrying out of these projects.

After having reviewed the actions of the International Congresses of Experimental Cytology at Stockholm and of Microbiology at Copenhagen and those to take place later in 1947 under the auspices of IUBS (Symposia on Trace Elements in Plants and on Biological Antagonisms), the following program of activities was established for 1948 and 1949: *International Congresses*—Genetics (Stockholm), Entomology (Stockholm), Zoology (Paris), Silkworm Culture (Ales (Gard)), Physiology and Pathology of the Reproduction of Animals (Milan); *Symposia*—Bases of Nomenclature and of Systematic Botany (Utrecht), Terminology of Genetics and Cytology (Stockholm), Interaction of Egg and Sperm (Milan), Embryological Chemistry (Berne), Development and Regeneration of Nerves (probably in the United States).

There were also proposed: (1) Symposia on the Role of Anaerobes in Nature, on Nomenclature in Zoology and Entomology, and on Evolution in Biology; (2) Publication of a Catalogue of Type Specimens of Animal Species and of Historical Collections; (3) Distribution of Artificial Radioactive Isotopes for Experimental Biology; (4) Creation of a Center of Marine Biology in the Malay Archipelago; and (5) Formation of an Association of Directors of European Botanical Gardens.

Finally the Assembly approved unanimously the resolution transmitted to it by the Congress of Microbiology with regard to prohibiting all means of biological warfare. This resolution had been adopted by

...clamation at the final Plenary Session ...f the Fourth International Congress of ...Microbiology held in Copenhagen July 26: ..."The Fourth International Congress of ...Microbiology joins the International ...Society of Cell Biology in condemning in ...he strongest possible terms all forms of ...biological warfare. The Congress considers ...uch barbaric methods as absolutely un...worthy of any civilized community and ...rusts that all microbiologists throughout ...he world will do everything in their ...power to prevent their exploitation."

The next Assembly will take place in ...950, probably at Stockholm. The In...ternational Union of Biological Sciences ...nvites all countries not at present ad...hering to join the Union in the interests of ...cience in general and of each country in ...particular.

For all information address the Secre...tary General, Prof. P. Vayssiere, 57 Rue ...Cuvier, Paris Ve, France.

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The **American Type Culture Collection,** located at Georgetown University School of Medicine for the past 10 years, is to be established soon in a laboratory of its own at 2029 M Street; N. W., Washington 6, D. C. The staff will consist of **Ruth E. Gordon,** curator, **Isabel Christison,** mycologist; **Ruth Davis,** bacteriologist; and **Katherine Alvord,** secretary and business manager. **Ralph St. John-Brooks,** retired curator, National Collection of Type Cultures, Lister Institute, London, and present permanent secretary, International Association of Microbiologists, and collaborator, Centre de Collection de Type Microbiens, is returning from Switzerland in November and will occupy an office in the new laboratory. The task of examining the 4,000 cultures of the Collection for viability and purity, begun in 1944, is nearly finished. A complete catalogue of the American Type Culture Collection strains will be published as soon as possible after the appearance of the 6th edition of Bergey's Manual.

**The figuring of the 200-inch telescope mirror** was completed October 3, its parabolic surface reaching perfection within two millionths of an inch, according to the results of John A. Anderson, who has been in charge of the optical work, Ira S. Bowen, director, Mount Wilson Observatory, and members of the Observatory Council, who devised new methods of testing the mirror surface to check the accuracy of previous testing methods. The giant disc, weighing about 20 tons before the grinding, and larger than the floor of a two-car garage, was cast in 1935 by the Corning Glass Works and shipped to the California Institute of Technology the following spring. Five and one-quarter tons of glass were removed in the grinding and polishing of the mirror, under the direction of Marcus H. Brown. The disc will now be aluminized and mounted in the observatory built for it on the top of Mount Palomar in California, 130 miles southeast of Pasadena. It is expected that the telescope will be in operation by early summer of 1948. Both the Mount Palomar and the Mount Wilson Observatories will be operated jointly by the California Institute of Technology and the Carnegie Institution of Washington.

**The first foreign shipment of radioisotopes** produced from the atomic pile at Clinton Laboratories, Oak Ridge, Tennessee, left September 5 for the Commonwealth X-Ray and Radium Laboratory, Melbourne, Australia. The shipment, which consisted of 20 millicuries of phosphorus 32 for treatment of an urgent case of polycythemia vera, was made by air since phosphorus 32 has a half-life of only 14.3 days.

**At the High Plains Potato Conference** held in Monte Vista, Colorado, on August 15, a new organization, the Intermountain Plant Pathologists, was formed by 12 plant pathologists from that region. Through the society plant pathologists of the Intermountain Region will be able to maintain closer contact with each other with respect to plant disease problems in the region and thus more effectively attempt to solve such problems. Membership in the society, an unofficial branch of the American Phytopathological Society, is open to plant pathologists in Idaho, Montana, Nebraska, Wyoming, Utah, Colorado, New Mexico, and Arizona. W. D. Thomas, Jr., of Colorado A & M College, is chairman of the group for the coming year; W. J. Henderson is secretary.

**A new observatory** for the daily determination of the radiation of the sun at sea level is now being set up at Miami, Florida, as a part of the program of the Smithsonian Institution's Astrophysical Observatory, directed by **L. B. Aldrich.** Other similar observatories under Smithsonian direction are located on the tops of Mt. Montezuma in Chile, and Table Mountain in California, where the amount of heat radiation from the sun is least affected by dust or water vapor in the atmosphere. The Miami station, however, where the atmosphere is considerably more dense, will be an especially desirable place for studying the effects of the absorption by water vapor. The new station will also cooperate with the Army in measuring the effects of solar radiation on various fabrics. Mr. Aldrich is now looking for another high mountain site in Mexico for an observatory to replace one recently abandoned at Tyrone, New Mexico.

**Clinton Laboratories,** at Oak Ridge, Tennessee, which have been operated since July 1945 by the Monsanto Chemical Company, are to be renamed Clinton National Laboratory and, under the terms of a four-year contract now being negotiated, will henceforth be operated by the University of Chicago. The Laboratory will thus become the third of AEC's national laboratories. The first to be established, Argonne National Laboratory, also operated by the University of Chicago, has as participants 29 institutions throughout the Midwest, while Brookhaven National Laboratory, operated by Associated Universities, Inc., is composed of 9 eastern universities. At Clinton 14 southern universities in the Oak Ridge Institute for Nuclear Studies and a score of industries and industrial representatives will participate in the research, development, and training programs. This plan of establishing national laboratories, conceived by Manhattan District's Advisory Committee on Research Policy, has as a major objective the utilization of research personnel and facilities of industry and academic institutions throughout the country and institution of a program of training in the nuclear sciences. The Oak Ridge Institute for Nuclear Studies, headed by Frank P. Graham, president, University of North Carolina, and formed last year to promote activities in nuclear science in southern universities, includes as members Alabama Polytechnic Institute, Catholic University of America, Duke University, Emory University, Georgia School of Technology, Louisiana State

University, Tulane University, the Universities of Alabama, Kentucky, North Carolina, Tennessee, Texas, and Virginia, and Vanderbilt University.

**The National Registry of Rare Chemicals,** 35 West 33rd Street, Chicago 16, Illinois, lists the following wanted chemicals: 6-hydroxy-2,2,5,7,8-pentamethylchroman; d-2-desoxyribose; hydrocoerulignone; diborane; deuteroammonia; coniferin; nitroarginine; agmatin; galegin; canaline; canavanene; hydroxylysine; laudanosine; 3-chloropyridazine; pyridazone; pyridazone-3-carboxylic acid; pyridazinone-3-carboxylic acid; xanthopterin; desoxypyridoxine; ethionine; carbon oxyselenide; and carbon sulfoselenide.

**The Huancayo Magnetic Observatory,** the most important of its kind in this hemisphere, has now been transferred to the Government of Peru from the Carnegie Institution of Washington, in accordance with the latter's policy of transferring fixed observatories to the governments of countries in which they are located, and also in accordance with the recommendation of the International Union of Geodesy and Geophysics that governments take over such facilities within their own territory because of their importance to national economy. The Observatory, functioning autonomously, will be supervised by a Directive Committee headed by Jorge Broggi, director, Geological Institute of Peru, and including three Peruvian scientists, and three U. S. representatives: J. M. Hydrick, Rockefeller Foundation, and now of the Peruvian Ministry of Public Health; John A. Fleming, formerly director, Department of Terrestrial Magnetism, Carnegie Institution, and currently special adviser to the Institution in international scientific affairs, who led in the establishment of the Observatory in 1922; and the cultural attaché of the U. S. Embassy in Peru.

## The Swedish Deep Sea Expedition

The Swedish Deep Sea Expedition, organized by, and under the personal direction of, Hans Pettersson, director of the Oceanografiska Institutet, left Göteborg on July 4, 1947, on the 1,450-ton motor schooner *Albatross*. The trip is expected to last approximately 15 months, and during that time oceanographic studies will be conducted in low-latitude regions in the Atlantic, the Caribbean, the Pacific, the Indian Ocean, and the Mediterranean. On August 20, 1947, the *Albatross* had reached the Canal Zone and was scheduled to proceed to Tahiti via the Galapagos and Marquesas Islands, thence to Hawaii and the Netherlands East Indies, and through the Indian Ocean to the Mediterranean.

The principal work of the expedition is to obtain cores of sediment in the deep ocean basins. These are taken with the new piston core sampler developed by Börje Kullenberg, and undisturbed cores have been obtained up to 20 meters in length. The events recorded in these deep-sea cores should greatly add to our meager knowledge of the recent history of the oceans, and such long cores may extend a few millions of years into the geologic past when obtained from the center of a large ocean basin. In addition to cores, continuous depth records are made with a new type of British fathometer which records on a larger scale than any other at present in use. Depth profiles from the Atlantic basins show a remarkable roughness of the bottom in the deep basins in many places with several abrupt changes in depth suggesting fault zones. Waloddi Weibull is measuring the apparent thickness of the deep ocean sediments by means of sonic reflections recorded from the explosion of small depth bombs. In the Caribbean Weibull has obtained a probable thickness ranging from 1,000 to 3,000 feet. Complete hydrographic stations are being occupied at regular intervals, and the intensity of light penetration is being measured at various depths. Large water samples also are being collected from deep water layers for a study of their radioactivity.

It was the good fortune of the undersigned to be the guest of the expedition on its way from Martinique to the Canal Zone, representing the Hydrographic Office of the Navy Department and the Woods Hole Oceanographic Institution. Towing techniques for living Foraminifera were demonstrated, and a new type of bottom sampler was loaned to the party. The *Albatross* is admirably fitted out for a round-the-world cruise, and the scientific party and ship officers and crew are of the highest degree of competence. The ship is a freighter and merchant officer training ship with the midship section converted into laboratories and quarters for the scientific staff. On the main deck is a large general laboratory as well as a chemical and biological laboratory. On the second deck is a large laboratory for treating the cores, which are opened on board, a large refrigeration room for the preservation of certain materials, an aquarium room, a completely equipped photographic dark room, and a small machine shop. The large winch for operating the piston core sampler is in the forward hold and is equipped with 7,500 meters of unspliced heavy cable.

It is interesting to note that the cost of the expedition (approximately $500,000) is not being borne by the government of Sweden, but is made up entirely of donations from private Swedish citizens who are interested in sponsoring the pure science of oceanography. This is a remarkable achievement for a country having only about 4 per cent of the population and 1 per cent of the wealth of the United States and now being subjected to severe income taxation. There is no doubt that the Swedish Deep Sea Expedition will produce results which are of fundamental importance to oceanography. (FRED B. PHLEGER, JR., *Woods Hole Oceanographic Institution.*)

**Erratum.** The price of *Thermodynamics for chemists* by Samuel Glasstone was incorrectly quoted in its review by Don M. Yost in *Science*, September 26. The book is a single volume, not one of a series, and its correct price is $5.00.

## Make Plans for—

**American Institute of Electrical Engineers,** Midwest General Meeting, November 3–7, Chicago, Illinois.

**American Institute of Chemical Engineers,** November 9–11, Detroit, Michigan.

**National Committee for Mental Hygiene,** November 12–13, Hotel Pennsylvania, New York.

**American Society of Animal Production,** November 28–29, Chicago, Illinois.

**The Society of American Foresters,** Annual Meeting, December 18–20, Minneapolis, Minnesota.

**American Association for the Advancement of Science,** 114th Meeting, December 26–31, Chicago, Illinois.

# COMMENTS
## *by Readers*

**The undersigned welcome this opportunity to discuss the questions raised by Dr. Potter** (*Science*, October 10, p. 342), which will be taken up under the separate numbers which he has listed:

(1) Whether or not there is a relative unsaturation of cytochrome C within the cell is unknown, since the answer to this question is not accessible to direct experimental proof. We suggested a possible excess of cytochrome oxidase over cytochrome C in the tissues on the basis of the following data:

From the saturation curve of Stotz, Altschul, and Hogness (*J. biol. Chem.*, 1938, **124**, 744) it was calculated how much cytochrome would be required to saturate the amount of oxidase indicated by the oxygen consumption of various tissues under the conditions of the assay method for cytochrome oxidase. These values were compared with the amounts of cytochrome actually found in various tissues by Potter and DuBois (*J. biol. Chem.*, 1942, **142**, 417). Stotz, Altschul, and Hogness stated that in their saturation curve the velocity of cytochrome oxidation and not that of its reduction is the limiting factor. According to the authors, the oxygen uptake at the end of the measurement accounted at each point of the curve for maximally 25 per cent of the cytochrome C. Thus, even assuming a slow re-reduction, at least 75 per cent of cytochrome C was still present in the reduced form at the time of the reading. The assay method for cytochrome oxidase is likewise carried out under conditions under which the rate of cytochrome oxidation is the limiting factor.

It is very likely that the application of such simplified calculations to the conditions of the living tissues ignores important factors such as that of the structure or of the influence of other metabolites. On the other hand, it appears to be of interest to compare the available quantitative data concerning the isolated cytochrome oxidase-cytochrome C complex with the assay figures obtained on various tissues. Actually, our physiologic and clinical experiments with cytochrome C are independent of these theoretical calculations. This should not, however, preclude attempts to interpret the available data in a preliminary manner.

(2) We have been intrigued by the question of whether or not the injected cytochrome C penetrates to the inside of the cells, but we have made no statement to the effect that it does. While we have demonstrated that the cytochrome C contents of some organs are increased following parenteral injection, there is as yet no evidence that cytochrome C, being a protein and hence a fairly large molecule, can penetrate cell membranes and thus take part in intracellular activities. The increase in organ content of cytochrome C is considerably more than can possibly be accounted for by the increased content in the circulating blood which resulted from the injection. If the material does not reach the interior of the cells, it might conceivably accumulate in the tissue spaces or perhaps on the surface of the cells. The fact that it does influence physiologic behavior, however, suggests that the cytochrome C probably does enter the cells. If it were assumed a priori that the cytochrome C molecule is too large to be physiologically active after parenteral injection, then one might with equal logic assume that insulin, which is a much larger molecule, or a host of other substances of large molecular weight, could not be effective. Such effectiveness probably indicates cellular penetration.

(3) In our experiments an attempt was made to control the "dilution factor" by adding sufficient cytochrome C to the control vessel to render the concentration of cytochrome C in the total homogenate equal to that in the undiluted tissue.

(4) We have reported (a) that under the conditions of our experiments (2) anoxia reduces the amounts of the easily hydrolyzable phosphorus of rat organs (hearts and kidneys), and (b) that the previous injection of cytochrome C seems largely to prevent this decrease. While Scheinberg and Michel (*Science*, April 4, pp. 365–366) also found that anoxia would reduce the amounts of easily hydrolyzable phosphorus in rat organs, they were unable to confirm our observations on the cytochrome C effect in overcoming some of this reduction. This led us to repeat our own experiments on rat hearts. Our subsequent results were essentially as originally reported by us. That Scheinberg and Michel did not obtain similar results, although presumably using essentially the same procedure and methods, suggests the desirability of clarification of this question by other workers for, as Dr. Potter states, "this experiment would be decisive if it could be confirmed."

Dr. Potter has suggested that there is some question as to whether our technique of fixing the tissues was sufficiently quick to preserve the phosphorus compounds and implied that we should have used the method of freezing by liquid air. The method which we employed was the immediate homogenization of the quickly excised organ in ice-cold trichloracetic acid. The advantages of freezing in liquid air are at least equivocal for two reasons. First, freezing by air is not instantaneous through any considerable depth of tissue; there is a significant gradient. Second, the immersion of a muscle into liquid air acts to stimulate the muscle to maximal contraction and thus fixes it not in the metabolic stage prior to immersion, but in an extraneously produced physiologic condition. It is very likely that a similar stimulatory effect occurs in other organs.

(5) We feel, as Dr. Potter does, that the question as to whether or not cytochrome C is of any therapeutic value will have to be answered on the basis of the results of investigators in a number of clinics. It is notoriously difficult to evaluate therapeutic effects in many clinical conditions, a good example being angina pectoris, which is one of the conditions we have been studying. The only clinical condition in which we have had any considerable experience with cytochrome C therapy is intermittent claudication. In 26 of 39 such patients there seem to have been significant measurable benefits. It may well be that the mechanism of this benefit is entirely different from that which we have presupposed. Even so, our working hypothesis has not been without value.

We, too, are interested in seeing a sufficient body of facts accumulated by qualified and impartial observers so that the true status of the results of our tentative explorations can be determined. The pharmaceutical houses can be helpful by supplying the material necessary to obtain these facts. (SAMUEL PROGER, G. SCHMIDT, and D. DECANEAS, *Joseph H. Pratt Diagnostic Hospital, Tufts College Medical School, Boston.*)

# TECHNICAL PAPERS

## Effect of Rutin on Anaphylactic and Histamine Shock[1]

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In the anaphylactic shock in man and in animals histamine plays an important role, but its liberation does not explain all phenomena observed (*1*). The discovery of rutin as an important tool to affect capillary permeability has given us the means to analyze the role played by capillary permeability in the shock produced in the guinea pig by anaphylaxis and by the administration of histamine.

Medium-sized guinea pigs were sensitized by an intraperitoneal injection of 0.25 cc. of normal horse serum. After a 12-day interval the animals were shocked by a parenteral dose of horse serum.

*Series I* consisted of 8 animals. These were sensitized and then divided into two groups. Three animals received 2 mg. of rutin intraperitoneally 30–45 minutes before anaphylactic shock was produced. The crystalline rutin was dissolved in 2 per cent NaOH to which 2 per cent acetic acid was added carefully to a point just short of precipitation. The solution was then diluted with distilled water to a volume convenient for injection. The above procedures had to be performed while maintaining the solutions at a temperature below 15° C. to prevent degradation of the rutin. Reaction at higher temperatures was indicated by color changes in the solution.

All animals were then given intracardially a shocking dose of 0.05 cc. of normal horse serum /100 grams body weight. The 3 animals which had received a prior injection of rutin manifested no symptoms. The 5 retained as controls died within 6 minutes, exhibiting the characteristic syndrome of anaphylactic shock in the guinea pig.

*Series II* consisted of 11 animals sensitized in the previously described manner. These were divided into two groups, one of which, consisting of 5 animals, received 1 mg. of rutin intraperitoneally 30–45 minutes before shocking. The control group received intraperitoneal injections of the same quantity of NaOH and acetic acid solution as used in dissolving the rutin for the first group.

Shocking doses of 0.5 cc. of normal horse serum were administered intracardially to all animals. The 5 which had received rutin showed no signs of shock, while the 6 controls died in 4–10 minutes with typical symptoms of anaphylactic shock.

*Series III* (11 animals) was subjected to procedures identical with those of Series II except that the solvent for rutin used here was propylene glycol, 0.5 cc. /dose. The controls received injections of the same amount of propylene glycol only.

In this series the 5 controls again died in anaphylactic shock within 10 minutes. Five of the 6 rutinized animals were without signs of anaphylactic shock, while the sixth, which received its shocking dose 60 minutes after the administration of rutin, died in anaphylactic shock in about 15 minutes. Whether this increased time interval between the administration of rutin and its apparent failure to protect is significant has not as yet been determined.

After finding that rutin protected against anaphylactic shock, presumably through its action on capillary permeability, we proceeded to examine the effects of rutin on the shock produced by histamine.

Of a batch of 21 guinea pigs, 6 animals were used to determine the minimal lethal dose of histamine dihydrochloride (donated by Hofmann-LaRoche) injected intracardially or intravenously. Nine animals were given 1 mg. of rutin in 0.1 cc. of propylene glycol intraperitoneally 30–45 minutes before receiving the minimal lethal dose of histamine. The 9 controls received only the propylene glycol.

All animals in both series died within 10 minutes after administration of the histamine, exhibiting the characteristic symptoms of histamine shock.

Our results demonstrate that rutin protects guinea pigs against the fatal effects of anaphylactic shock but not against those of histamine shock. If we assume that rutin protects against anaphylactic shock by virtue of its tightening effect on the capillary endothelium, then histamine may be excluded as the lethal factor of anaphylactic shock. However, in the guinea pig in anaphylactic shock, the dominating picture is that of bronchiolar constriction. In guinea pigs injected 30–45 minutes before the induction of anaphylactic shock with rutin, no spasm of the bronchioles was apparent, and their lungs were found to be normal. On the other hand, injected histamine produced the syndrome of protein anaphylactic shock with bronchiolar spasm and changes in the lungs. A clinical difference between shock induced by either anaphylaxis or by injection of histamine was hardly recognizable.

Another explanation for the protective effect of rutin may be that it prevents the liberation of endogenous histamine, perhaps by unknown factors other than those which increase capillary permeability. The latter explanation seems to be more reasonable because its protective effects on anaphylactic shock are of rather short duration, while its effectiveness on capillary permeability in purpuric disease seems to be more protracted. The latter thought may be sustained also by the findings of Hiramatsu (*2*), who found that guinea pigs were protected against anaphylactic shock by large doses of hesperidin. While the latter preparation may have contained some vitamin P, it may have prevented the liberation of endogenous histamine in a manner similar to that of rutin. Hiramatsu did not report whether hesperidin protected against histamine shock.

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[1] Aided by a grant from the Gusta M. Rothschild Fund. The Department is in part supported by the Michael Reese Research Foundation.

# Ammonia Nitrogen Produced From Isomeric Peptides in Kidney Homogenate Digests

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On aerobic incubation of glycyl-*dl*-alanine and of *dl*-alanylglycine with aqueous homogenates of rat kidney tissue, we noted that considerable ammonia accumulated in digests of the former peptide while little or none appeared in those of the latter. Essentially similar findings were observed with isomeric peptides of *dl*-leucine (Table 1). Of further interest was the fact that the ammonia which appeared in digests of glycyl-*dl*-alanine and of glycyl-*dl*-leucine was close in order of magnitude to that which appeared in digests of *dl*-alanine and *dl*-leucine, respectively. Of the isomeric tripeptides studied, only glycylglycyl-*dl*-leucine yielded ammonia.

TABLE 1

AMMONIA N PRODUCED FROM PEPTIDES AND AMINO ACIDS IN AEROBIC DIGESTS OF RAT KIDNEY HOMOGENATES*

| Substrate | Hours of incubation | Ammonia N in micromoles† |
|---|---|---|
| *dl*-Alanine | 4 | 6 |
| " | 8 | 10 |
| Glycyl-*dl*-alanine | 4 | 6 |
| " | 8 | 10 |
| *dl*-Alanylglycine‡ | 4 | <1 |
| " | 8 | 1 |
| *dl*-Leucine | 4 | 5 |
| " | 8 | 9 |
| Glycyl-*dl*-leucine | 4 | 5 |
| " | 8 | 9 |
| *dl*-Leucylglycine | 4 | <1 |
| " | 8 | 1 |
| *l*-Leucine | 4 | 1 |
| Glycyl-*l*-leucine | 4 | 1 |
| Glycine | 8 | 0 |
| Glycylglycine | 8 | 0 |
| *dl*-Valine | 4 | 5 |
| *dl*-Isovaline | 4 | 0 |
| *dl*-Leucylglycylglycine | 4 | 0 |
| Glycyl-*dl*-leucylglycine | 4 | 0 |
| Glycylglycyl-*dl*-leucine | 4 | 5 |
| *d*-Leucylglycine§ | 4 | 0 |
| *d*-Leucylglycine + 0.001 M $MnCl_2$ | 4 | 1 |
| *d*-Leucylglycine + Mn + *l*-leucine | 4 | <1 |
| *d*-Leucylglycylglycine | 4 | 0 |
| *d*-Leucylglycylglycine + 0.001 M $MnCl_2$ | 4 | 0 |

*Digests consisted of 1 cc. of dialyzed homogenate equivalent to 333 mg. of tissue, plus 2 cc. of 0.15 M borate buffer at pH 8.1, plus 1 cc. of 0.05 M racemic or 0.025 M optically active substrate. Enzymatic activity was measured by the amount of ammonia produced, corrected for the extract blanks. No ammonia was produced from any substrate when the digestion was conducted under anaerobic conditions. Temperature, 37° C.

†Theoretical maximum, 25 micromoles from each optically active component.

‡Chloroacetyl-*dl*-alanine and chloroacetylglycyl-*dl*-leucine in similar aerobic digests yielded no ammonia N.

§ $[\alpha]_D = -82°$.

[1] Rockefeller Foundation Fellow, on leave from the University of Brazil, Rio de Janeiro.

The ammonia which appears from the racemic substrates under these experimental conditions is due principally to *d*-amino acid oxidase activity and may be related specifically to the oxidative desamination of the *d*-amino acid moiety of the peptides (*5*). Neither *l*-leucine nor glycyl-*l*-leucine yields appreciable ammonia under these conditions. That the oxidative desamination involves the $\alpha$-$\beta$ hydrogen atoms of the substrate is revealed in the relative susceptibility of *dl*-valine and of *dl*-isovaline (Table 1). The latter possesses a tertiary carbon atom. Manometric procedures of estimating peptidase activity through amino acid oxidase have been reported (*4, 7*).

The contribution of the *l*-amino acid components to the yield of ammonia in digests of the racemic, isomeric peptides may therefore be relatively neglected, and the role of the natural *l*-peptidase in the splitting of the *l*-form of the peptides in the kidney digests is not of immediate concern in the interpretation of the phenomena. This leaves for consideration only the *d*-form of the peptides, namely, *d*-alanylglycine and *d*-leucylglycine on the one hand, and glycyl-*d*-alanine and glycyl-*d*-leucine on the other. Two alternative explanations for the behavior of the isomeric peptides may be offered.

(1) *d*-Amino acid oxidase may be considered as acting only on free *d*-amino acids, and therefore the ammonia noted in digests of the racemic peptides could only have arisen subsequent to the action of *d*-peptidase on the peptides liberating the free amino acids. On this basis, it would appear that glycyl-*d*-alanine and glycyl-*d*-leucine were very susceptible, whereas *d*-alanylglycine and *d*-leucylglycine were relatively resistant, to the action of *d*-peptidase. This would not be in agreement with the relative susceptibility of the corresponding *l*-peptides to intestinal dipeptidase, whereby alanylglycine is hydrolyzed at twice the rate as glycylalanine (*6*). A slight, but definite, manganese-activatable *d*-leucylpeptidase activity is noted in the rat kidney digests (Table 1) (cf. *7*). This activity is slightly depressed by the addition of *l*-leucine.

(2) *d*-Amino acid oxidase may be considered as acting not only on the free *d*-amino acids, but also upon *d*-amino acids bound through the amino group in peptide linkage with another amino acid. Such a concept is in harmony with Bergmann's view that the oxidative desamination of amino acids might be effected while they are in the peptide chain, yielding by an $\alpha$-$\beta$ dehydrogenation the corresponding dehydropeptide, which subsequently is split by dehydropeptidases to products which include ammonia and keto acids (*1*). Thus:

$$(1)\quad RCH(NH_2)CONHCH(CH_2R^1)COOH \xrightarrow[\text{Oxidase}]{-2H} RCH(NH_2)CONHC(=CHR^1)COOH \xrightarrow[\text{Dehydropeptidase}]{H_2O} RCH(NH_2)COOH + NH_3 + CH_2R^1C(=O)COOH$$

$$(2)\quad 2H + O \rightarrow H_2O.$$

On this basis, dipeptides which contain a glycine residue at the carboxyl end of the chain, as in alanylglycine and leucylglycine, could not form dehydropeptides, whereas peptides like glycylalanine and glycylleucine could form such $\alpha$-$\beta$ unsaturated peptides. Kidney tissue is, of all animal tissues, richest in both *d*-amino acid oxidase (*5*) and dehydropeptidase (*2*).

The second of these alternatives was sympathetically considered by Krebs in his early work on the subject of amino acid oxidation, but no decision was reached by him (*5*). On the basis of our present data, we are inclined to favor this second alternative, which is not only consistent with the Bergmann concept of intracellular peptide metabolism, but also supplements earlier work from this laboratory on the enzymatic susceptibility of peptides of *l*-cystine (*3*). In the final analysis, however, the Bergmann concept can only be proved by separation of the enzymes involved, and work on this possibility is in progress.

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## Use of Insoluble Penicillin Salts for the Prolongation of Penicillin Blood Levels


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Many methods have been proposed for prolonging blood levels of penicillin. The one usually employed in medical practice is that proposed by Romansky and Rittman (*3*), namely, an intramuscular injection of a suspension of calcium penicillate in beeswax and a vegetable oil. This method has the disadvantage of using a substance (beeswax) of variable composition which may not in all cases be completely absorbable.

In a search for a method of prolonging penicillin blood levels, the writer decided to investigate the insoluble penicillin salts. These compounds have not been used until now becau se it was believed that the penicillin in such salts was irreversibly inactive. Thus, Abraham and Chain (*1*) found that penicillin was inactivated by a large number of metallic ions—copper, lead, zinc, cadmium, nickel, mercury, and uranium. They also reported that no activity could be recovered by decomposing the inactivated material with acid and extracting with ether. Bacharach and Hems (*2*) state that zinc, copper, mercury, and lead inactivate penicillin rapidly and iron less rapidly. Whether this inactivation is due to the formation of an insoluble penicillin or whether there is a definite chemical change in the penicillin is a subject for future investigation.

It occurred to the writer that there was a possibility that the inactivated insoluble penicillin might be reactivated *in vivo*. If this proved to be true, the insoluble salt would be more slowly absorbed than the soluble sodium, potassium, and calcium salts now in use and would therefore result in a marked prolongation of blood levels. Moreover, all the substances used would be completely absorbable. These suppositions were correct, as shown by the following data.

A control intramuscular injection in a rabbit of 20,000 units/kg. of penicillin suspended in peanut oil gave no readable blood level after 5 hours. On the other hand, a similar injection of silver penicillate produced a blood level of .08 units/cc. at 17 hours and .03 units at 20 hours; one of mercury penicillate, a level of .08 units at 17 hours and one of ferric penicillate, a level of .16 at 17 hours and .02 at 20 hours.

Penicillin produces insoluble salts with iron, copper, tin, vanadium, lead, lanthanum, cesium, zirconium, mercury, bismuth, silver, gold, and probably many other metals. Insoluble salts are also obtained with numerous organic substances, basic or cationic in character, such as the triphenylmethane dyes, namely, gentian violet, brilliant green, crystal violet, methyl violet, and basic fuchsin; with the acridine dyes such as acriflavine and proflavine; with Nile blue, malachite green, toluylene red, safranine, quinine, quinidine, cinchonine, cinchonidine, and hyamine 1622.

The reactivation of penicillin *in vivo* takes place not only with inorganic but also with organic salts. An intramuscular injection in a rabbit of 20,000 units/kg. of brilliant green penicillate produced a blood level of .16 units/cc. at 18 hours, and a similar injection of gentian violet penicillate, a blood level of .04 units at 18 hours.

A more detailed report will appear elsewhere.

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## Inhibition of the Enzymatic Hydrolysis of ATP by Certain Cardiac Drugs[1]


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Although many investigations on the action of cardiac drugs have been carried out, only a few studies have dealt with their influence on the enzymatic reactions of heart muscle. Recently, however, Guerra, *et al.* (*2*) have reported that $1:10^6$ ouabain increased the liberation of inorganic phosphorus from adenosine triphosphate (ATP) as catalyzed by a cardiac muscle myosin preparation.

As part of a systematic investigation of the action of certain glycosides on enzyme systems we were interested in the effect of these drugs on the energy-yielding enzymatic reactions in connection with the therapeutic and toxic actions of these substances. The effect of digitoxin and ouabain *in vitro* on the ATP-ase activity of cardiac muscle was, therefore, studied, and the present preliminary report indicates that both of these drugs affect this enzymatic reaction.

ATP-ase activity was measured by the method of DuBois and Potter (*1*) using a Klett-Summerson colorimeter for phosphorus measurements. Normal Sprague-Dawley rats averaging 200 grams were employed. Aqueous solutions of ouabain were added to give a final concentration of $6 \times 10^{-5}$ M, and 10 per cent alcoholic solutions of digitoxin were added in amounts sufficient to give a final concentration of $4.7 \times 10^{-6}$ M.


[1] This work was supported by a grant from the Life Insurance Medical Research Fund and the Dr Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.


[2] Lederle Laboratories Research Fellow.

In order to ascertain whether the action of the drugs was due to an action on the enzyme or on calcium, the activator for this enzyme, the effect of digitoxin was studied in the presence of suboptimal quantities and an excess of calcium. Table 1 shows the effect of varying amounts of calcium on the ATP-ase activity of normal rat's heart. It may be seen that with quantities of calcium below 0.003 M the reaction rate was limited by the calcium concentration. The results presented in Table 2 indicate that a final concentration of $4.7 \times 10^{-6}$ M digitoxin inhibited the ATP-ase activity of cardiac muscle, the decrease in ATP-ase units being nearly the same, regardless of the calcium concentration. The per cent inhibition decreased with increasing calcium concentrations, since calcium increased both the control and digitoxin-treated samples to the same extent.

TABLE 1

RELATIONSHIP OF CALCIUM CONCENTRATION TO PER CENT STIMULATION OF ATP-ASE ACTIVITY

| Molar $CaCl_2$ | ATP-ase units | Stimulation (%) |
|---|---|---|
| 1. 0.0003 | 14.20 | 66 |
| 2. (None) | 8.54 | |
| 1. 0.0006 | 14.43 | 78 |
| 2. (None) | 8.09 | |
| 1. 0.003 | 21.32 | 222 |
| 2. (None) | 6.62 | |

TABLE 2

RELATIONSHIP OF DIGITOXIN ($4.7 \times 10^{-6}$ M) TO PER CENT INHIBITION OF ATP-ASE ACTIVITY

| Molar $CaCl_2$ | ATP-ase units | | Decrease in ATP-ase units | Inhibition (%) |
|---|---|---|---|---|
| | Control | Drug | | |
| 1. 0.0003 | 14.20 | 11.09 | 3.11 | 21.90 |
| 2. 0.0006 | 14.43 | 11.64 | 2.79 | 19.33 |
| 3. 0.003 | 21.32 | 18.61 | 2.71 | 12.71 |

Ouabain also inhibited the ATP-ase system. In the presence of 0.003 M calcium, ouabain ($6 \times 10^{-5}$ M) produced 13.8 per cent inhibition. A higher concentration of ouabain than digitoxin was, therefore, necessary to produce a similar inhibitory effect.

These experiments indicate that both digitoxin and ouabain inhibit the ATP-ase activity of normal rat cardiac muscle. The amount of inhibition was independent of the calcium concentration, indicating that the drugs did not act through interference with the metallic activator. The difference in the per cent inhibition with various amounts of calcium indicates that the drugs inhibited a dephosphorylation reaction not dependent upon calcium ions for activity. With a limiting amount of calcium, an excess of ATP-ase is present in the test system to react with the drug, and less inhibition would be expected than in the case where the ATP-ase is limiting the reaction rate. The similarity in the decrease of ATP-ase units, regardless of whether calcium or ATP-ase was limiting the reaction rate, indicates that the drugs were inhibiting a dephosphorylation reaction not catalyzed by ATP-ase.

Further studies are necessary on other phosphatases in order to elucidate this inhibitory action of cardiac drugs.

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# Creatinuria in Diabetics and an Evaluation of Methods for Determining Total Creatinine


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Diabetics exhibit an above-normal blood sugar, and when the blood sugar rises above the renal threshold there occurs a spilling of the sugar into the urine. In this disease the muscle glucose and glycogen are low and manifest a low tissue carbohydrate metabolism. It is probable that other metabolites present in these tissues in excess of the reduced metabolic requirements will also be found spilled into the urine.

Creatine plays a role in cellular metabolism and proliferation (*2*) as well as in muscular contraction (*4*). A low muscle content of carbohydrate and creatine would account for a reduced metabolism and for the muscular fatigue and degeneration which follows the course of this disease.

Creatine found in the urine of a number of diabetic subjects of both sexes was determined by the method of Folin (*3*). In

TABLE 1

| Age group | No. of subjects | Average creatine (mg./day) |
|---|---|---|
| 32–37 | 3 | 487 |
| 43–48 | 21 | 670 |
| 50–53 | 18 | 790 |
| 32–53 | 42 | 649 |

Table 1 appears a summary of the average creatine spilled during 24 hours. In this series the low excretion of creatine was found to be 176 mg./day, and the high was approximately 1,600 mg./day.

Albanese and Wangerin (*1*) reported that in the Folin total creatinine determinations there occurs a decomposition loss of creatinine equivalent to 8 per cent when samples are autoclaved 20 minutes and 9 per cent when they are autoclaved 40 minutes. In order to obtain a more accurate creatine estimation in urine, they proposed a modification which involves autoclaving the standard as well as the preformed creatinine urine.

It seems to us that the loss of creatinine upon autoclaving does not appear to be great in view of the admitted error of ± 10 per cent in the technique involving an optical colorimeter. It is essential to determine in practice whether the Albanese modification will account for the loss of creatinine by the Folin method. By comparing identical samples of the autoclaved urine with the autoclaved as well as nonautoclaved standards of creatinine and creatinine zinc chloride, we will obtain indications of the direction and magnitude of the error

in the Folin method. Any autoclaved urine sample should yield a lower creatinine level when compared with the nonautoclaved standard than when compared with the autoclaved standard.

One ml. of a 24-hr. specimen of urine was mixed with 20 ml. of a saturated picric acid and autoclaved for 20 minutes. The solution was then cooled, and 1.5 ml. of a 10 per cent NaOH solution was added. The mixture was allowed to stand 10 minutes, after which it was diluted to volume. The creatinine standards were dissolved in dilute HCl. One creatinine standard was autoclaved with picric acid; the other was not. All solutions were compared and read in a photoelectric colorimeter. A few samples of urine and creatinine standards were autoclaved 40 minutes. The results of the total creatinine found in the various urines are given in Table 2.

TABLE 2

TOTAL CREATININE DETERMINATIONS BY METHOD OF ALBANESE

| Urine sample | Calculated from autoclaved (20 min.) | | Calculated from nonautoclaved | | | |
|---|---|---|---|---|---|---|
| | Creatinine standard (mg./ml.) | Creatinine zinc chloride standard (mg./ml.) | Creatinine standard (mg./ml.) | Deviation (%) | Creatinine zinc chloride standard (mg./ml.) | Deviation (%) |
| (Autoclaved 20 min.) | | | | | | |
| H 83 | 1.36 | 1.36 | 1.37 | +0.7 | 1.33 | −2.2 |
| C 51 | 1.00 | 0.99 | 1.00 | 0.0 | 1.02 | +3.0 |
| K 13 | 0.88 | 0.88 | 0.89 | +1.1 | 0.88 | 0.0 |
| C 64 | 1.27 | 1.26 | 1.28 | +0.8 | 1.33 | +5.5 |
| A 2 | 0.54 | 0.54 | 0.55 | +1.8 | 0.55 | +1.8 |
| A 7 | 1.75 | 1.74 | 1.76 | +0.6 | 1.77 | +1.7 |
| A 1 | 1.23 | 1.23 | 1.20 | −2.4 | 1.20 | −2.4 |
| B 2 | 1.91 | 1.93 | 1.88 | −1.5 | 1.87 | −3.1 |
| B 3 | 0.92 | 0.93 | 0.91 | −1.1 | 0.91 | −2.1 |
| B 9 | 1.80 | 1.81 | 1.76 | −2.2 | 1.76 | −2.8 |
| B 10 | 1.47 | 1.48 | 1.52 | +3.4 | 1.52 | +2.7 |
| K 88 | 1.56 | 1.56 | 1.60 | +2.5 | 1.60 | +2.5 |
| (Autoclaved 40 min.) | Standards autoclaved 40 min. | | | | | |
| A 1 | 1.17 | 1.17 | 1.18 | +0.9 | 1.18 | +0.9 |
| B 2 | 1.83 | 1.83 | 1.85 | +1.1 | 1.85 | +1.1 |
| B 3 | 0.89 | 0.89 | 0.90 | +1.1 | 0.90 | +1.1 |
| 8 | 1.31 | 1.31 | 1.30 | −0.8 | 1.30 | −0.8 |

The deviation in results obtained with a nonautoclaved creatinine standard as compared with an autoclaved standard varied from −2.4 to +3.4 per cent, and more than 50 per cent of the determinations were higher when compared with the nonautoclaved standards than when compared with the autoclaved standards.

*Summary:* Creatinuria was found in all 42 diabetic clinic subjects of both sexes taken at random.

Total creatinine determined in the urines of diabetics by the Albanese modification showed a variable deviation (in magnitude and direction) when compared with total creatinine obtained by the Folin method.

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# Interpretation of Lignin: The Synthesis of Gymnosperm Lignin

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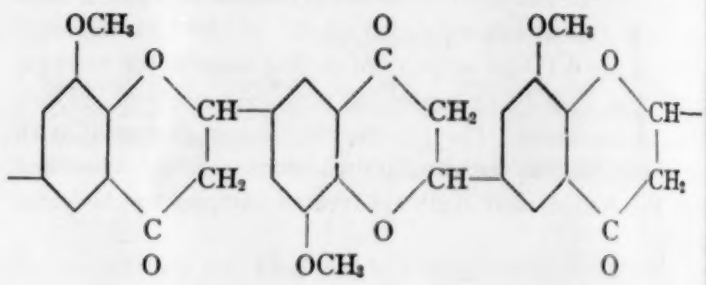
The existence of at least two varieties of lignin appears to be definitely established. One is associated with gymnosperms and gives, as significant fission products, only derivatives of catechol monomethyl ether (guaiacol). The other is associated with angiosperms and gives, as significant cleavage products, the same derivatives of catechol monomethyl ether and also some derivatives of pyrogallol-1,3-dimethyl ether. The possible occurrence of varieties of lignin giving other fission products is not excluded.

Examination of the analytical evidence accumulated during the past 70 years, excludes the improbable elaborate formulas previously proposed and leads to the conclusion that the lignin from gymnosperms is a polymeric 8-methoxy-dihydrobenzopyrone having the structure:



(I)

The lignin from angiosperms is likely constituted in a similar way but having pyrogallol-1,3-dimethyl ether nuclei terminally or otherwise attached or introduced. Such nuclei obviously could not replace directly the catechol monomethyl ether nuclei in (I) unless the migration of a methyl group occurs during degradation.

The material (I) is a cyclicized condensation (aldolization, loss of water—Claisen condensation) polymer of 2-hydroxy-3-methoxy-5-formylacetophenone (III) and is at once available by Fries rearrangement of vanillin monoacetate (II) through the steps (II) (III) (IV) (I).

This synthesis has been accomplished and the amorphous synthetic product, although somewhat darker in color, is qualitatively indistinguishable from a specimen of the lignin from gymnosperms. It has to give the same fission products, and its solubility characteristics and general behavior are the same. Moreover, absorption curves for the synthetic and the natural product are in agreement, and, so far as such comparisons are valid for amorphous materials, quantitative analytical measurements of the synthetic material and its derivatives are in harmony with calculated values and with the reported values for the lignin from gymnosperms.

For comparison purposes an exactly similar synthesis was carried out starting with p-acetoxybenzaldehyde. The product is analogous to that obtained from vanillin monoacetate.

It is to be noted that, in the above synthetic work, use has

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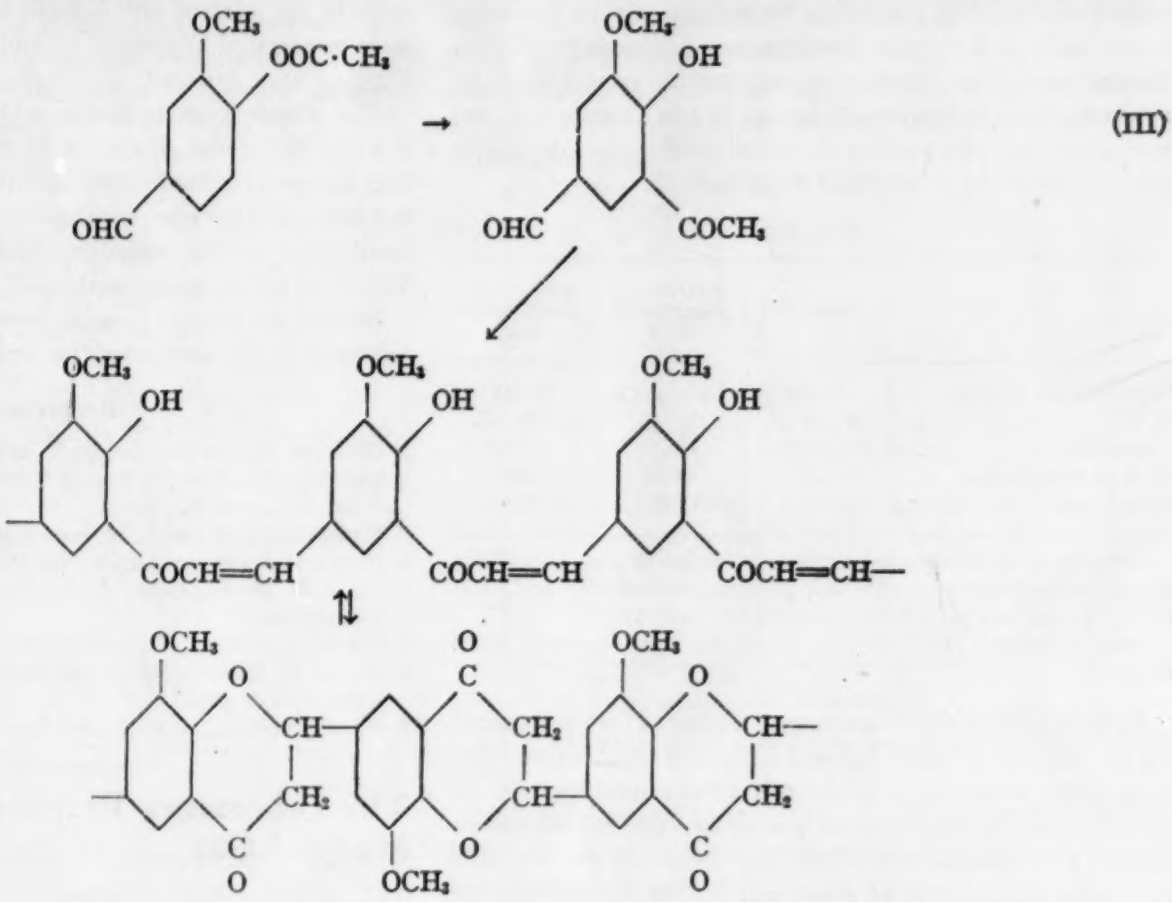
een made of a new type of polymerization reaction—the olymerization of a monomeric bifunctional ketoaldehyde. In hydroxyl groups present, materials built on the polydihydrobenzopyrone model would likely have tanning properties. It is




(III)

hese cases the reaction amounts to a condensation polymeriation, but it could, in other cases, be an addition process.

If water solubility were achieved by having enough phenolic conceivable that natural phlobatannins have just such a structure.

A detailed report of this work will appear elsewhere.

# IN THE LABORATORY

## Ortho-Hydroxyphenylacetic Acid From an Amorphous Penicillin

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Recently Welch, Randall, and Price (*6*) have directed the interest of antibiotic investigators toward the significance of some impurities in certain batches of amorphous commercial penicillin. By means of a biological assay technique (*7*) which they developed these investigators were able to determine the presence of a nonpenicillin component which enhanced the activity of crystalline penicillin. Hobby, Burkhardt, Hyman, and Levert (*4*) have also demonstrated the presence of an enhancement factor in certain lots of impure penicillin.

This laboratory undertook the task of isolating and identifying the constituents in a batch of the amorphous commercial penicillin in which Welch, *et al.* had found the enhancement factor.

Since the material described by Welch, *et al.* as containing the enhancement factor was shown to be acidic by these authors, and in view of our previous results in the application of partition chromatography to the resolution of the penicillins (*2*, *3*), this technique was applied to the present problem. An investigation of numerous buffer and solvent systems finally resulted in the use of the subsequent conditions as the method of choice.

The crude penicillin was extracted four times at room temperature from an aqueous pH 2 buffer solution into ether, and the combined ethereal phases were evaporated to dryness, thus destroying any penicillin present. The residue was taken up in chloroform and added to a prepared chromatographic column in which silicic acid was the adsorbent and a 20 per cent potassium phosphate buffer of pH 3.6 the immobile solvent. The precautions mentioned in an earlier report (*2*) were followed in the preparation of the column. The chromatographic fractions subsequently referred to include the colorless as well as the colored zones on the column. With chloroform as the initial mobile solvent, 10 zones were eluted from

the column. Ether was then substituted as the mobile solvent, and two additional bands were collected. Finally, an ether-butanol mixture (9:1) resulted in the development of two more zones. Each of the above fractions was analyzed by Welch, Randall, and Price (7) by their method for ascertaining the presence of the enhancement factor. A small amount of enhancement was exhibited in the third fraction, but the major portion was found in fractions 9 through 12.

TABLE 1

| | Unknown | p-Hydroxy-phenylacetic acid | o-Hydroxy-phenylacetic acid |
|---|---|---|---|
| $FeCl_3$, test for phenols | Violet | Light green | Violet |
| M. P. | 149–150° C. | 150° C. | 149–150° C. |
| Neut. equiv. | 150.2–151.6 | 152.06 | 152.06 |
| M. P. of methyl ether | 124 | 85–86 | 124 |
| Methyl ester | 71–71.5 | Oil | 71.0 |

Mixed M. P. of unknown and p-hydroxyphenylacetic acid, 122–135° C.; of o-hydroxyphenylacetic acid and p-hydroxyphenylacetic acid, 122–135° C.; of unknown and o-hydroxyphenylacetic acid, 148° C.

*Anal.* Calculated for $C_8H_8O_3$: C, 63.13; H, 5.30. *Found:* C, 62.95; H, 5.78.

Sufficient quantities of fractions 9 through 12 were prepared for the purpose of purifying and identifying the active principle. After evaporation of the solvent the residues were all glass-like and varied from an amber to dark reddish-brown color. Crystallization was effected by dissolving the free acid in a minimum amount of ether and adding enough benzene or petroleum ether to bring the system to a point just short of precipitation or, if precipitation occurred, the mixture was heated slightly to clarify and crystallization initiated at room temperature. Depending on the type of crystallization employed, either needles or rosettes of needle-like crystals were recovered. A series of recrystallizations were required in order to achieve clean, white crystals exhibiting a sharp melting point at 149–150°C. From the physical and chemical tests to which the unknown and derivatives of the unknown were subjected, it became evident that either p- or o-hydroxyphenylacetic acid was the compound involved. A sample of p-hydroxyphenylacetic acid was obtained through the courtesy of Chas. Pfizer & Company, and a sample of o-hydroxyphenylacetic acid was synthesized in this laboratory. These two compounds and their derivatives were compared with the unknown and its derivatives. The data in Tables 1 and 2 demonstrate conclusively that the crystalline component separated from the active fraction of the crude penicillin used is o-hydroxyphenylacetic acid.

TABLE 2

INFRARED DATA

(Absorption Bands in Microns)

| Unknown | o-Hydroxyphenylacetic acid | p-Hydroxyphenylacetic acid |
|---|---|---|
| 13.75 | 13.75 | 12.60 |
| 13.18 | 13.18 | 12.10 |
| 11.75 | 11.75 | 11.95 |
| 11.42 | 11.42 | 11.62 |
| 10.60 | 10.60 | 11.09 |
| 10.32 | 10.32 | 10.41 |
| 7.85 | 7.85 | 9.80 |

For the sake of brevity only the significant differences between the absorption bands of o- and p-hydroxyphenylacetic acids in the infrared are included in Table 2. The compounds were mascerated in mineral oil and the mixture analyzed in a Perkin-Elmer infrared spectrophotometer.

The o-hydroxyphenylacetic acid was prepared by a modification (5) of the procedure of Czaplicki, von Kostanecki and Lampe (1). Preliminary experiments with o-hydroxyphenylacetic acid have not conclusively demonstrated an enhancement effect on the penicillin blood levels. These studies by Welch, *et al.* are being continued.

Studies are now in progress toward the isolation and identification of the component in active "fraction 3."

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## The Laboratory Preparation of Mustard Gas


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The current interest in mustard gas in producing gene mutations suggests the desirability of describing a convenient procedure for making and handling this material. Because of shipping restrictions it is easier to make mustard in the laboratory than to buy it. The wide variation in susceptibility to mustard between individuals or in the same individual after repeated exposures makes the handling of the material an important consideration.

Mustard can conveniently be prepared by warming $\beta\beta'$-dihydroxy ethyl sulfide (Eastman Kodak No. T1224) with concentrated hydrochloric acid. The reaction can be followed by observing the separation of a heavy oil which settles to the bottom. In practice we have used a large excess of acid in order to drive the reaction to completion. Twenty-five ml. of the $\beta\beta'$-dihydroxy ethyl sulfide may be heated with 75 ml. of concentrated hydrochloric acid at 60° C. for 30 minutes. A longer time will do no harm. The aqueous layer is then poured off, the oil being washed rapidly with a little distilled water and transferred to a storage bottle. This preparation should be carried out in a hood with good ventilation, the aqueous layer poured into a cream of bleaching powder to destroy any mustard, and the hands washed promptly with bleaching powder to remove any mustard absorbed from the gas phase.

The flask shown in Fig. 1 is convenient for storing, since it permits one to remove a sample without contaminating the air of the laboratory from the storage flask. If an aspirator is turned on before the first stopper is taken out, the downcurrent of air will sweep away any mustard diffusing out of the flask when the second stopper is removed. We have used cork stoppers covered with metal foil, since mustard is readily

sorbed by rubber. In fact, rubber tubing will completely move mustard from an air stream, only to give it off later hen the tube is more or less saturated.

The easiest way to obtain a given partial pressure of mustrd in an air stream is probably to make a saturator by taking U-tube, inserting a folded filter paper in each arm in such

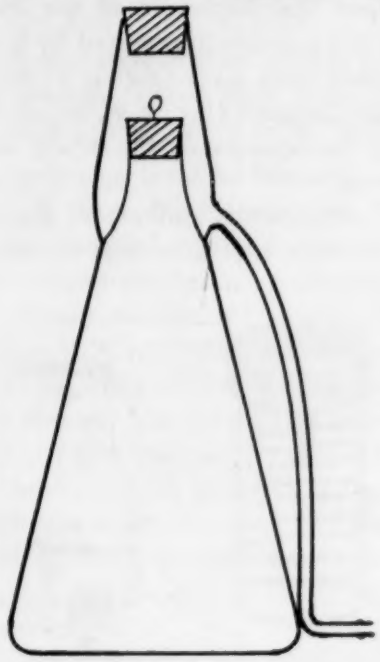

FIG. 1

way as to give a large surface, and then pouring in enough ustard to dampen the filter paper by capillary rise. This U-tube can then be put in a beaker of water of any desired emperature below room temperature to give the desired artial pressure. We have recently submitted to the *Journal of the American Chemical Society* an article giving vapor pressure data on mustard which fit the equation $\log_{10}p = 9.4819 - 3117.2/(t + 273.1)$, in which p is the vapor pressure in millimeters and t is the centigrade temperature.

## Oxidation of β-Carotene With Osmium Tetroxide

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The successful oxidation of carotene at the central double bond to form vitamin A aldehyde, accomplished by Hunter and Williams (*3*) using hydrogen peroxide, indicated that a catalyst was necessary to improve their low yield (0.5 per cent). Osmium tetroxide, used by Criegee (*1*) for the oxidation of anethole and other ethylenic compounds, seemed to have the characteristics of being such a substance, since, with hydrogen peroxide, both aldehydes and glycols are formed (*4*).

If one of the central double bonds can be formed into the epioxide simultaneously with formation of a diglycol at the other, then the resulting compound is identical with the postulated intermediate of the Cannizzaro reaction. This, according to Fredenhagen and Bonhoeffer (*2*), undergoes rearrangement prior to fission, which would account for β-carotene having half the biological value of vitamin A by weight, and corresponding lower values for other provitamin A compounds.

In applying the reaction of Criegee it has been found that a 1 per cent ethereal solution of osmium tetroxide cannot be prepared from the solid and kept, as it is all reduced in a few hours. An aqueous solution has therefore been employed. Similarly, 30 per cent hydrogen peroxide (aqueous) has been used, although in both cases the reaction proceeds faster with a slightly higher yield if the solutions used are anhydrous in the initial stages.

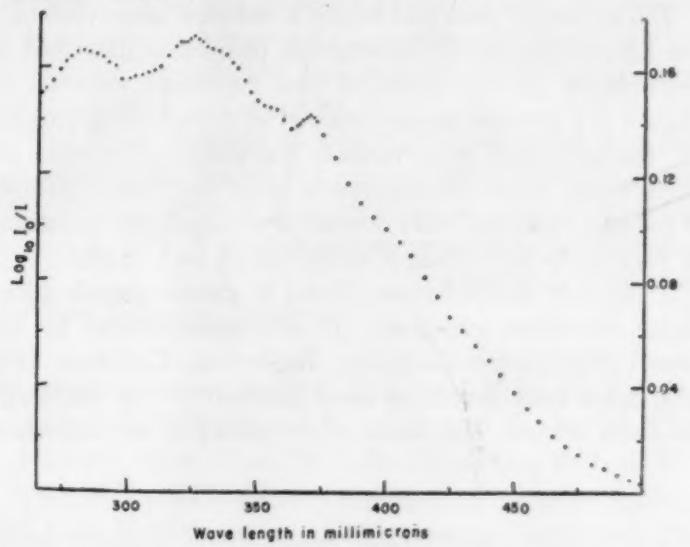


FIG. 1. Absorption curve of oxidation products of β-carotene in cyclohexane.

This work is still in progress, and the details will be published at a later date. However, a typical set of conditions for the reaction is as follows:

About 10 grams of anhydrous sodium sulfate is introduced into a 500-ml., three-necked flask fitted with a reflux condenser, a sealed stirrer, and a burette. For the initial stages the reflux condenser should be fitted with a loosely packed, calcium chloride drying tube. A 50-ml. aliquot of a solution of carotene (90 per cent β- and 10 per cent α-carotene) in anhydrous, alcohol-free ethyl ether is run in from the burette, followed by 1 ml. of a 2 per cent aqueous solution of osmium tetroxide, the solution is stirred for 5 minutes or until a color change is observed, and 2 ml. of 30 per cent hydrogen peroxide is then introduced dropwise. The solution is stirred for 10 minutes, 3 ml. of a 0.5M sodium bicarbonate solution is added slowly, and the stirring is continued until there is no further effervescence. A mixture of 50 ml. of 95 per cent ethyl alcohol and 5 ml. of 50 per cent potassium hydroxide solution is added. The solution is stirred for a further 10 minutes, then decanted into a 500-ml. separatory funnel, and 50 ml. of ethyl ether is added. The funnel is then shaken thoroughly, the lower layer run off, and the supernatant washed as in vitamin A analysis.

An aliquot of the resulting solution is dried over anhydrous sodium sulfate, evaporated under reduced pressure, and taken up in cyclohexane. The absorption spectrum of this solution shows maxima at 283, 325, and 370 mμ (Fig. 1). If the intensity of the blue color with antimony trichloride, measured at 620 mμ, is due to vitamin A, the yield is 30–40 per cent of the theoretical conversion of β-carotene to vitamin A.

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# An Improved Electromagnetic Sphygmograph[1]

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The apparatus described here is a technical improvement of the Electromagnetic Sphygmograph previously described by the authors (*1*), but differs in two important respects: (1) the use of a dynamic speaker magnet in the recording unit and (2) the placement of a variable resistor in series with the microphone. These improvements make for greater stability of the apparatus and make it possible to obtain sphygmograms of practically any desired amplification and clarity.

A 200-ohm, single-button, Model W carbon granule microphone, described previously (*1*) and manufactured by Universal Microphone Company, Inglewood, California (Fig. 2,7), has a light aluminum knob fastened to the diaphragm by Duco cement. This knob, when placed on any superficial

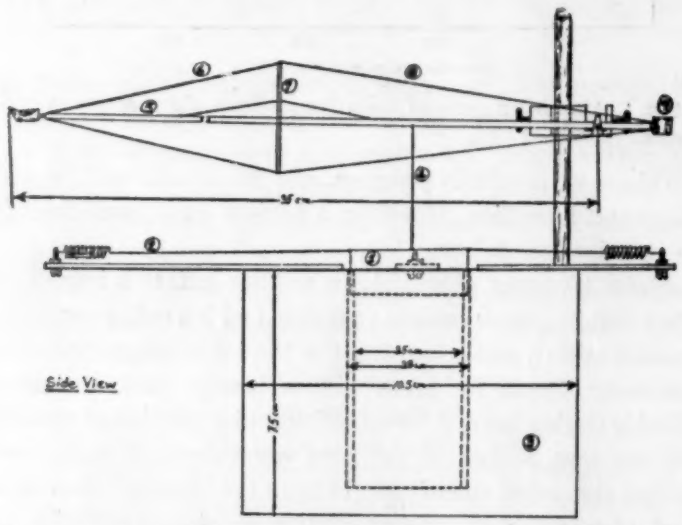


FIG. 1. The improved Electromagnetic Sphygmograph: (1) movable coil —25 turns of #28 enameled wire; (2) flexible radial support with adjustable spring tension; (3) dynamic speaker magnet; (4) stiff connecting wire; (5) wood heart lever; (6, 7, 8) stiffening members; (9) adjustable counterbalance.

artery, serves to transmit to the diaphragm the fluctuations in pressure of the pulse-pressure waves. Since the internal resistance of the microphone varies with the pressures exerted on the diaphragm, the fluctuations in pressure caused by the pulse beat are converted into corresponding fluctuations of resistance. Since the current through the microphone is a function of its internal resistance, in accordance with Ohm's law, $I = E/R$, the fluctuations of pressure are ultimately converted into corresponding pulsations of current. The voice coil of a 20-watt dynamic speaker, consisting of 25 turns of #28 enameled wire (Fig. 1, 1; Fig. 2, 1), is connected in series with the microphone. As shown in Fig. 2, the pulsating current passes through the movable coil, suspended in the magnetic field of a *dynamic speaker magnet* (Fig. 1, 3) by means of three adjustable radial supports (Fig. 1, 2). The possibility of using a permanent magnet speaker field suggests itself here.

The pulsations of current cause the movable coil to move up and down through the magnetic field of the speaker magnet by an amount which is at any time directly proportional to the pressure the artery is exerting, through the layers of surrounding tissues, upon the diaphragm of the microphone. The movements of the coil are transmitted by a stiff wire (Fig. 1, 4) to a trussed heart lever (Fig. 1, 5) equipped with an adjustable counterbalance (Fig. 1, 9), which then accurately transcribes the movements of the artery on an ordinary kymograph drum.

In order to regulate the strength of the current flowing through the movable coil, a *variable resistor* (Fig. 2, 2)

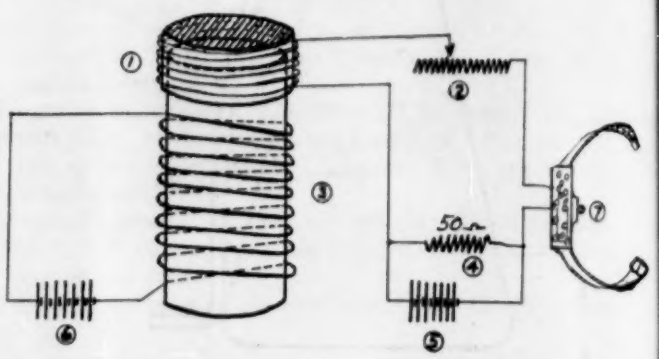


FIG. 2. Wiring plan: (1) movable coil; (2) variable resistance in series; (3) radial field winding and core; (4) 50-ohm damping resistance in parallel; (5) battery for microphone and movable coil circuit; (6) battery for field circuit; (7) microphone with adjustable straps.

placed in series with the microphone-movable coil circuit. The amplitude of the recording can be regulated by varying the resistance. Ideal records for all subjects tested were obtained with the resistor set at values from 50 to 200 ohms when the system is used in conjunction with a 6-volt battery (Fig. 2, 5).

FIG. 3. Typical sphygmograms: top to bottom—normal radial, normal carotid, normal radial (strong amplification).

A 50-ohm damping resistor (Fig. 2, 4) is placed in parallel with the microphone circuit in order to assure a "dead beat" movement" of the coil and hence a "damping down" of the rebounds of the writing lever. Both the field magnet and the microphone-coil circuit are energized by an ordinary 6-volt, wet-cell battery or, preferably, separate batteries should be used for each circuit, as shown in Fig. 2, 5, 6.

As seen from the sphygmograms (Fig. 3), clear and well-defined transcriptions of practically any desired amplitude may be obtained with this apparatus from the carotid, radial, or any of the other superficially located arteries.

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[1] From a paper read by Baldwin before a section meeting of the Society for Experimental Biology and Medicine, San Diego, June 1947.

[2] Present address: Department of Physiology, School of Medicine, Stanford University.

[3] The assistance and cooperation of R. E. Vollrath, of the Department of Physics, is gratefully acknowledged.

# Book Reviews

***A new notation and enumeration system for organic compounds.*** G. Malcolm Dyson. New York-London-Toronto: Longmans, Green, 1947. Pp. iv + 63. $1.75.

This monograph presents the fundamental portions of a new notation which, in the words of the author, "may go far towards advancing those difficulties of chemical nomenclature that, as chemistry advances, become more apparent each year, particularly in classification and indexing. . . . The scheme was first formulated in 1944, and various tests were carried out to ascertain, as far as could be done at that time, the general validity of the system. The Ring Index was completely ciphered into the new notation, and it was found that there was no single entry which did not give a unique and unequivocal cipher. Five volumes of Beilstein were ciphered into the new notation, and these have been collated and arranged in cipher-index order; and in no case did the system fail to provide a satisfactory delineation."

Complete details are given for translating organic compounds into the appropriate cipher. The compounds covered include: hydrocarbons, alcohols, glycols, and phenols; ethers; epoxy compounds; aldehydes and ketones; quinones; carboxylic acids; carboxylic esters; lactones; heterocyclic compounds; amines; acid amides, halides, and anhydrides; nitroso, nitro, and azido compounds; ureas, urethanes, etc.; azo compounds; hydrazines, oximes, etc.; halogens; sulfur compounds; phosphorus compounds; carbohydrates; and polysaccharides. In the appendix are given ciphers for some steroids (adrenal) steroids (general), aporphine alkaloids, morphine alkaloids, and fused rings. Included also are ciphers for compounds numbered 2401 to 2700 in the Ring Index.

Acyclic and alicyclic hydrocarbons are all delineated in terms of 6 symbols, as follows: C, carbon; E, double bond; $E_1$, cis arrangement at the double bond; $E_2$, trans arrangement at the double bond; $E_3$, triple bond; A, bridge or ring. The number following the letter C gives the number of carbon atoms in the longest straight carbon chain in the molecule. The cipher for 2,2-dimethyl-5-methyl-7-propyldecane is C10.4C3.6C2.9,9C. For 1,3-butadiene, the cipher is C4.1,3E. Cycloparaffin rings are denoted by the letter A, as AC4 for cyclobutane, AC5 for cyclopentane, AC6 for cyclohexane, etc. Cyclohexane with a bridge-link in the 1–3 position is AC6.1-3A. Cyclooctane with two bridge-links, in the 1–5 and 3–7 positions, each bridge comprising a single methylene group, is AC8.1-5,3-7AC.

All aromatic and fused rings are ciphered in terms of the following conventional rings: V, cyclopentadienyl; B, benzene; W, indenyl; K, naphthalene; J, phenanthrene; T, anthracene. Other fused rings are derived from these 6 fundamental rings by the addition of fragments of the benzene ring or of saturated chains. The fragments are called adducts. For example, the Beilstein notation, 4′.4″.Dimethyl-(dibenzo-1′.2′:2.3;1″.-2″:6.7 phenanthrene) becomes T9.6,21C.

The Dyson system is readily applicable to punched-card manipulation, is well suited for indexing purposes, but appears to have some limitations with regard to classification purposes. The accuracy of any cipher can be checked independently by computing the molecular formula from the cipher, using constants supplied by the author.

The Dyson cipher is an important contribution in the field of indexing and classifying compounds, and those concerned with this type of work should familiarize themselves with this system so that all possible advantage may be taken of it.

FREDERICK D. ROSSINI

*National Bureau of Standards*

***Psychiatric research.*** C. K. Drinker, J. Folch, S. Cobb, H. S. Gasser, W. Penfield, and E. A. Strecker. Cambridge, Mass.: Harvard Univ. Press, 1947. Pp. 113. (Illustrated.) $2.00.

This slender book is a very stimulating and timely collection of addresses prepared by six distinguished scientists. These were presented originally at the dedication of the Laboratory for Biochemical Research at the McLean Hospital on May 17, 1946. Opened in 1818, the McLean was the first institution for the care of the mentally ill in Massachusetts. Rufus Wyman was chosen by the Trustees of the Massachusetts General Hospital as its first director. The institution became outstanding for leadership in psychiatric care, and its research program did much to advance the field of scientific psychiatry. A paper by Cecil K. Drinker on "Research at the McLean Hospital" gives a concise review of the steps which there advanced psychiatric treatment and the research accomplished. The second paper, "Biochemical Problems Related to Psychiatry," is by Jordi Folch, director of scientific research at the McLean. Here is presented a thoroughgoing survey of brain function from the biochemical viewpoint, with special emphasis on problems which the author feels have been hitherto sometimes neglected. This discussion should be particularly useful to students entering this field. It includes some tabular material and provides a bibliography of 65 references.

The address by Stanley Cobb, entitled "Integration of Medical and Psychiatric Problems," presents a report of the psychiatric service at the Massachusetts General Hospital during the last five years. A new psychiatric ward was opened in 1941; and findings are reviewed for a group of 843 typical patients. The discussion concerns methods of treatment and typical outlines of laboratory investigations. A study of neurocirculatory asthenia is presented as an example of work in a problem field where integration between internal medicine and psychiatry has borne fruit in clinical investigations. The paper has a bibliography of 42 references.

The fourth chapter, entitled "Protocol for a Review of Psychiatry," by Herbert S. Gasser, will doubtless be provocative of much discussion. Propounding the theory that all of the sciences might have in common a strict type of language as exact as the language of physics, Dr. Gasser discusses the problem of bridging the hypothetical chasm in observation and semantics between the so-called natural and psychological sciences. He assumes that "as parts of science, psychiatry and

neurophysiology differ no more than their coefficients of complexity." Not infrequently in psychiatric writings a single sentence may contain a combination of nonintertranslatable terms from two languages: the language of the psyche and that of physics. Dr. Gasser asks whether the science of psychiatry might not develop most rapidly if its reports were so phrased as to bypass areas in which observation and subsequent exact communication have not so far been achieved. A brief review statement can hardly do justice to this chapter.

A chapter on "Psychical Seizures" by Wilder Penfield gives the clinical histories of some of his patients in an illuminating and well-illustrated review. This eminent specialist convincingly develops the view that many new fields of treatment would be open to the surgeon if he could but understand the nature of the problems and secure the cooperation of understanding colleagues in his own and related areas.

The final chapter by Edward A. Strecker, on "The Psychobiology of Psychiatric Research," presents psychiatric research as itself an organism passing through various mood-swings and changes of attitude and gradually making more and more satisfactory adjustments to the realities of mental disease.

The general tenor of all six addresses is forward-looking and constructive. The present reviewer closed the book with the strengthened conviction that psychiatry as a psychological science is destined to play a positive and important part in man's happier life adjustments. All the contributors to the present symposium have emphasized the point of view that progress in psychiatry will be made more effectively as this discipline becomes more soundly scientific. These contributions are blueprints that may well serve as guides to constructive scientific development.

This volume, published as No. 9 in the series of "Harvard University Monographs in Medicine and Public Health," is to be highly recommended for students in psychiatry and psychology and also for the more general reader.

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